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As filed with the Securities and Exchange Commission on May 13, 2019.

Registration No. 333-231076

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

Amendment No. 1
to

FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

BICYCLE THERAPEUTICS LIMITED*

(Exact Name of Registrant as Specified in Its Charter)

England and Wales	**2834**	**Not Applicable**
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

Bicycle Therapeutics Limited
B900, Babraham Research Campus
Cambridge CB22 3AT
United Kingdom
+44 1223 261503
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Bicycle Therapeutics Inc.
4 Hartwell Place
Lexington, Massachusetts 02421
Attention: Lee Kalowski
617-945-8155
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)

Copies to:

Kristopher D. Brown **James Xu** **Jonathan A. Schur** **Goodwin Procter LLP** **620 Eighth Avenue** **New York, NY 02109** **(212) 813-8800**	**Graham Defries** **Goodwin Procter** **(UK) LLP** **100 Cheapside** **London EC2V 6DY** **United Kingdom** **+44 20 7447 4200**	**Ed Lukins** **Edward Dyson** **Cooley (UK) LLP** **Dashwood** **69 Old Broad Street** **London EC2M 1QS** **United Kingdom** **+44 20 7785 9355**	**Divakar Gupta** **Richard Segal** **Ryan Sansom** **Cooley LLP** **55 Hudson Yards** **New York, NY 10001** **(212) 479-6000**

Approximate date of commencement of proposed sale to the public:
As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer o	Accelerated Filer o	Non-Accelerated Filer o	Smaller Reporting Company ☒ Emerging Growth Company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Calculation of Registration Fee

Title of each class of securities to be registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)(3)
Ordinary shares, nominal value £0.01 per share(4)	$79,733,328	$9,664

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act, as amended. Includes the aggregate offering price of additional ordinary shares represented by American Depositary Shares, or ADSs, that the underwriters have the option to purchase to cover over-allotments, if any.

(2) Calculated pursuant to Rule 457(o) under the Securities Act based on an estimate of the proposed maximum aggregate offering price.

(3) Previously paid.

(4) These ordinary shares are represented by ADSs, each of which represents one ordinary shares of the registrant. ADSs issuable upon deposit of the ordinary shares registered hereby are being registered pursuant to a separate registration statement on Form F-6.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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* We intend to alter the legal status of our company under English law from a private limited company by re-registering as a public limited company and changing our name from Bicycle Therapeutics Limited to Bicycle Therapeutics plc prior to the completion of this offering.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion. Dated May 13, 2019

4,333,333 American Depositary Shares

Representing 4,333,333 Ordinary Shares

bicycle therapeutics

This is an initial public offering of the American Depositary Shares, or the ADSs, of Bicycle Therapeutics plc. We are offering 4,333,333 ADSs. Each ADS represents one ordinary share, nominal value £0.01 per share.

Prior to this offering, there has been no public market for the ADSs or our ordinary shares. It is currently estimated that the initial public offering price per ADS will be between $14.00 and $16.00. We have applied to list the ADSs on the Nasdaq Global Market under the symbol "BCYC."

We are an "emerging growth company" as that term is used in the U.S. Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

See "Risk Factors" on page 15 to read about factors you should consider before buying the ADSs.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per ADS	Total
Initial public offering price	$	$
Underwriting discounts[(1)]	$	$
Proceeds, before expenses, to Bicycle Therapeutics	$	$

(1) See the section titled "Underwriting" for compensation payable to the underwriters.

To the extent the underwriters sell more than 4,333,333 ADSs, the underwriters have the option to purchase up to an additional 650,000 ADSs from us at the initial public offering price less the underwriting discounts.

Certain of our existing shareholders and their affiliated entities, including those affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $25.0 million of ADSs in this offering at the initial public offering price per ADS and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no ADSs to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no ADSs in this offering. The underwriters will receive the same underwriting discount and commissions on these ADSs as they will on any other ADSs sold to the public in this offering.

The underwriters expect to deliver the ADSs against payment in New York, New York on , 2019.

Goldman Sachs & Co. LLC **Jefferies** **Piper Jaffray**

Canaccord Genuity

Prospectus dated , 2019

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We have not, and the underwriters have not, authorized any person to provide you with information different from that contained in this prospectus or any related free-writing prospectus that we authorize to be distributed to you. This prospectus is not an offer to sell, nor is it seeking an offer to buy, these securities in any jurisdiction where the offer or sale is not permitted. The information in this prospectus speaks only as of the date of this prospectus unless the information specifically indicates that another date applies, regardless of the time of delivery of this prospectus or of any sale of the securities offered hereby.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the ADSs and the distribution of this prospectus outside of the United States.

ABOUT THIS PROSPECTUS

Prior to the completion of this offering, we intend to re-register Bicycle Therapeutics Limited as a public limited company and to change our name from Bicycle Therapeutics Limited to Bicycle Therapeutics plc.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms "Bicycle Therapeutics Limited," "Bicycle Therapeutics plc," "the company," "we," "us" and "our" refer to (i) Bicycle Therapeutics Limited and its wholly owned subsidiaries prior to the re-registration of Bicycle Therapeutics Limited as a public company, and (ii) Bicycle Therapeutics plc and its subsidiaries after the re-registration of Bicycle Therapeutics Limited as a public limited company, which shall occur prior to the completion of this offering. See "Share Capital Reorganization and Re-Registration" for more information.

We own various trademark registrations and applications, and unregistered trademarks, including our name and our corporate logo. All other trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective holders. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend to use or display other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PRESENTATION OF FINANCIAL INFORMATION

We maintain the books and records of Bicycle Therapeutics Limited, and its wholly owned subsidiaries in the United Kingdom, BicycleTx Limited and BicycleRD Limited in pounds sterling. For financial reporting, our results are translated to U.S. dollars and we prepare our consolidated financial statements in accordance with generally accepted accounting principles in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board. All references in this prospectus to "$" are to U.S. dollars and all references to "£" are to pounds sterling.

Unless otherwise indicated, certain pounds sterling amounts contained in this prospectus have been translated into U.S. dollars at the rate of $1.3032 to £1.00, which was the noon buying rate of the Federal Reserve Bank of New York on March 29, 2019, the last business day of the three months ended March 31, 2019. These translations should not be considered representations that any such amounts have been, could have been or could be converted into pounds sterling at that or any other exchange rate as of that or any other date. See "Exchange Rate Information" for more information.

We have made rounding adjustments to some of the figures included in this prospectus. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them. We have historically conducted our business through Bicycle Therapeutics Limited's subsidiaries, BicycleRD Limited, BicycleTx Limited and Bicycle Therapeutics Inc., and therefore our historical consolidated financial statements present the consolidated results of operations of Bicycle Therapeutics Limited. After the re-registration of Bicycle Therapeutics Limited into Bicycle Therapeutics plc and following the completion of this offering, our consolidated financial statements will present the consolidated results of operations of Bicycle Therapeutics plc.

PROSPECTUS SUMMARY

Overview

We are a clinical-stage biopharmaceutical company developing a novel class of medicines, which we refer to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint is designed to confer high affinity and selectivity and the relatively large surface area presented by the molecule allows targets to be drugged that have historically been intractable to non-biological approaches. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic, or PK, properties of a small molecule. *Bicycles* are excreted by the kidney rather than the liver and have shown no signs of immunogenicity to date, which we believe together support a favorable toxicological profile.

We have a novel and proprietary phage display screening platform which we use to identify *Bicycles* in an efficient manner. The platform initially displays linear peptides on the surface of engineered bacteriophages, or phages, before "on-phage" cyclization with a range of small molecule scaffolds which can confer differentiated physicochemical and structural properties. Our platform encodes quadrillions of potential *Bicycles* which can be screened to identify molecules for optimization to potential product candidates. We have used this powerful screening technology to identify our current portfolio of candidates in oncology and intend to use it in conjunction with our collaborators to seek to develop additional future candidates across a range of other disease areas.

Our initial internal programs are focused on oncology indications with high unmet medical need. Our lead product candidate, BT1718, is a *Bicycle* Toxin Conjugate, or BTC. This *Bicycle* is being developed to target tumors that express Membrane Type 1 matrix metalloprotease, or MT1-MMP. The *Bicycle* is chemically attached to a toxin that when administered is cleaved from the *Bicycle* and kills the tumor cells. BT1718 is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial in collaboration with, and fully funded by, the Centre for Drug Development of Cancer Research UK, or CRUK. We expect to report preliminary data from the Phase I part of this clinical trial in the second half of 2019. We are also developing BT5528 and BT8009, which are BTCs targeting Ephrin type-A receptor 2, or EphA2, and Nectin-4, respectively, for oncology indications. BT5528 and BT8009 are being investigated for safety, activity and to establish a rationale for therapeutic use in preclinical studies. We are currently conducting Investigational New Drug application, or IND, -enabling activities for BT5528 and BT8009. Our discovery pipeline in oncology includes *Bicycle*-targeted innate immune activators, as well as T-cell modulators.

Beyond oncology, we are collaborating with biopharmaceutical companies and organizations in therapeutic areas where we believe our proprietary *Bicycle* screening platform can identify therapies to treat diseases with significant unmet medical need. Our partnered programs outside of oncology include collaborations for anti-bacterial, cardiovascular, hematology, ophthalmology and respiratory indications.

We were founded in 2009 based on innovative science conducted by Sir Greg Winter and Professor Christian Heinis. Sir Greg Winter is a pioneer in monoclonal antibodies and, in 2018, was awarded a Nobel prize in chemistry for the invention of the technology underpinning our proprietary phage display screening platform that we use to identify *Bicycles*. Since our founding, we have generated substantial intellectual property, including three patent families directed to novel scaffolds, 11 patent families directed to our platform technology, 63 patent families directed to bicyclic peptides and related conjugates, and six patent families directed to clinical indications and other properties of development assets. The work we have conducted in developing *Bicycles* and

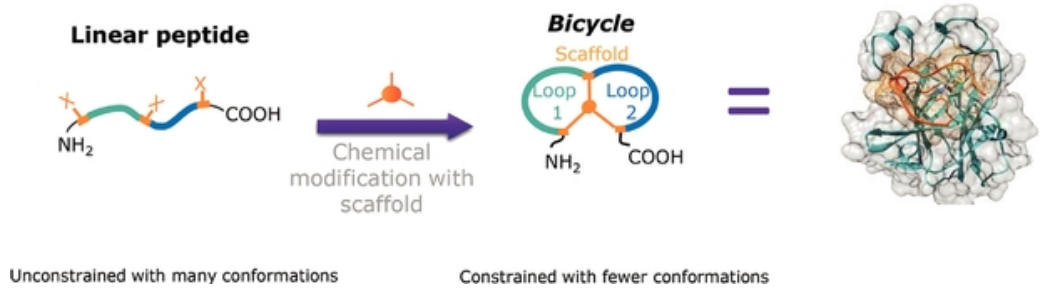
our proprietary screening platform have created substantial know-how that we believe provides us with a competitive advantage.

Introduction to *Bicycles*

Bicycles are fully synthetic, short peptides consisting of nine to 15 amino acids constrained to form two loops which stabilize the structural geometry of the peptide and facilitate target binding with high affinity and selectivity. *Bicycles* represent a unique therapeutic class, combining the pharmacological properties normally associated with a biologic with the manufacturing and PK advantages of a small molecule, with no signs of immunogenicity observed to date.

Drugs must bind to target proteins with high affinity and selectivity to achieve a therapeutic effect, while minimizing undesired effects on other proteins and physiological functions. Peptides exist in a number of folded states, only a few of which are able to bind to target proteins, and a key challenge for peptide therapeutics is designing structures that achieve these goals. We have designed our molecules to be highly constrained by linking a chemical connector compound, also known as a scaffold, to particular amino acids in the peptide chain. The resulting cyclized molecule, which we refer to as a *Bicycle*, is locked in the preferred state to bind to the target proteins.

Schematic of the Creation of a Cyclized Molecule Resulting in a Bicycle



We have expanded the diversity of the chemical space we can cover from approximately 10^{13} potential molecules in 2009 to 10^{17} today. We have applied our novel *Bicycle* modality to a growing range of targets, from a single target in 2009 to more than 90 today. We can create a wide range of *Bicycles* by varying four parameters:

- the number of amino acids in the two loops;
- the amino acid composition at each position;
- the symmetry of the two loops; and
- the small molecule scaffold used to cyclize the *Bicycle*.

Bicycles have a large surface area available for target binding, which is designed to allow high affinity and selectivity to the designated target. As short sequences of amino acids, or peptides, they have a low molecular weight, typically ranging from 1.5 kDa to 2.0 kDa. *Bicycles* have a readily adjustable PK profile with good plasma stability and rapid distribution from the vasculature into the extracellular space. This PK profile enables rapid tissue penetration and a renal route of elimination that minimizes liver exposure. Toxicity issues are observed with small molecules that are metabolized and eliminated by the liver. *Bicycle* peptides, by contrast, are not subject to metabolism or elimination by the liver but are metabolized in the peripheral circulation or kidney with subsequent rapid excretion in the urine. Consequently, by increasing excretion in urine, the liver exposure is minimized and the risk of liver toxicity is reduced. The modular nature of *Bicycles*

allows us to optimize therapeutic molecules for specific targets. To date, we have observed no signs of immunogenicity.

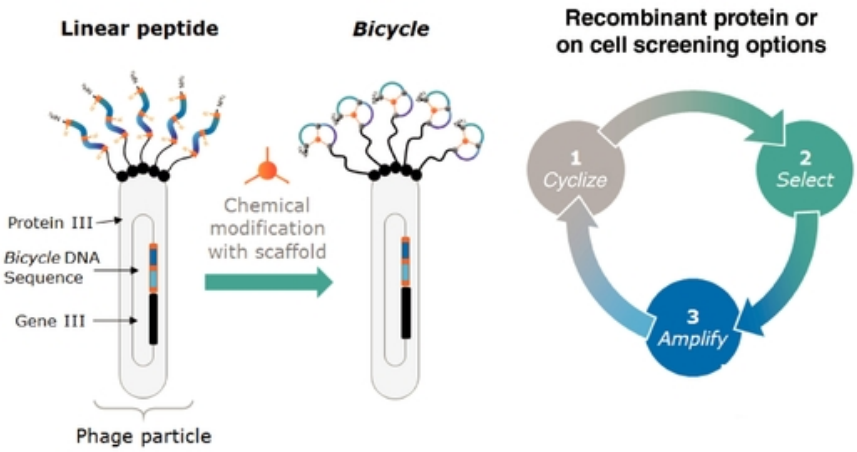
Compared to biologics, *Bicycles* have a lower cost of production and a simpler manufacturing process, and are recognized by regulatory authorities as small molecule new chemical entities. *Bicycles* can be readily identified to drug a wide spectrum of targets and target classes, including many that have so far been undruggable with small molecules, such as protein-protein interactions. Our novel and proprietary screening platform allows us to screen *Bicycles* against molecular targets quickly and efficiently, affording potentially reduced timelines and costs compared to other high-throughput screening approaches. Leveraging our platform, we can rapidly and efficiently identify a compound for development in only six to 12 months after a target has been selected.

Our Proprietary *Bicycle* Screening Platform

We utilize our novel and proprietary phage display screening platform to identify *Bicycles* that are potentially useful in medicine. We have used this technology to identify our current pipeline, and intend to leverage it to develop a broader portfolio of product candidates to address unmet medical needs across a wide range of diseases.

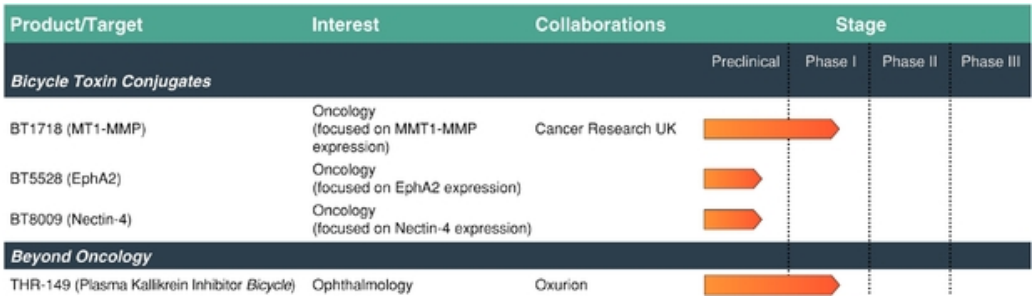
Our screening process self-selects for *Bicycles* that are amenable to attachment, commonly referred to as conjugation, to other molecular payloads such as cytotoxins, innate immune activators or other *Bicycles*. *Bicycles* can be linked together with synthetic ease to create complex molecules with combinatorial pharmacology. Alternatively, *Bicycles* in the form of multimers can also be used as standalone therapeutics, such as those that we are exploring in our T-cell modulator program. We believe that the flexibility of *Bicycles* and our powerful screening platform allow new therapeutics to be rapidly conceived and reduced to practice to potentially serve diverse therapeutic applications across a wide range of indications.

Schematic of our Proprietary Bicycle Screening Process



Our Pipeline

The following table summarizes key information about our pipeline programs.



***Bicycle* Toxin Conjugates**

BT1718

Our lead product candidate, BT1718, is a BTC that we are developing for oncology indications. The molecule is comprised of our MT1-MMP targeting *Bicycle*, a hindered disulphide cleavable linker and a cytotoxin payload of emtansine, or DM1.

MT1-MMP is a matrix metalloprotease involved in tissue remodeling and is generally expressed at relatively low levels in normal adult tissues. MT1-MMP has an established role in cell invasion and metastasis, and we believe that MT1-MMP is an attractive target for cytotoxin delivery due to its high level of expression on stromal and tumor cell subsets in various cancers, including breast, lung, sarcoma, gastric, bladder, endometrial, ovarian and esophageal cancers.

In our preclinical studies, we observed that BT1718 was associated with the greatest anti-tumor effect when membrane expression of MT1-MMP was high (as quantified by fluorescence activated cell sorting). Tumors with lower levels of expression of MT1-MMP were observed to have reduced levels of response to BT1718. We are collaborating with leading cancer researchers to determine MT1-MMP expression levels across a panel of tumor types, which will help inform patient selection for further clinical development. One of the goals of our clinical trials is to better understand the relationship between the level of target expression and activity of BT1718.

BT1718 is being investigated in an ongoing Phase I/IIa open label dose escalation and expansion clinical trial sponsored by CRUK. Up to 40 patients with advanced solid tumors are being enrolled in the ongoing Phase I part of this trial at three sites in the United Kingdom in which two dosing regimens are being evaluated. Once a recommended Phase IIa dose has been determined, the Phase IIa part of the trial is expected to commence.

BT5528

BT5528 is a BTC designed to target EphA2. The molecule is comprised of our EphA2 targeting *Bicycle*, a valine-citrulline, or val-cit, cleavable linker and a cytotoxin monomethyl auristatin E, or MMAE, payload.

EphA2 is a member of the Ephrin superfamily of receptor tyrosine kinases regulating cell migration, adhesion, proliferation and differentiation. EphA2 is expressed at relatively low levels in normal adult tissues but is overexpressed in numerous difficult to treat tumors including lung, breast, bladder, gastric, ovarian, endometrial, cervical, melanoma, esophageal, pancreatic, and

glioma. In both cell-derived and patient-derived preclinical models, we observed target-dependent anti-tumor activity signals following administration of our EphA2 toxin conjugates.

Our IND-enabling preclinical studies for BT5528 are currently ongoing.

BT8009

BT8009 is a BTC designed to target Nectin-4. The molecule is comprised of our Nectin-4 targeting *Bicycle*, a val-cit cleavable linker, and a cytotoxin MMAE payload.

Nectin-4 (also known as PVRL4) is a cell adhesion molecule from the Nectin and Nectin-like family, members of which are integral to the formation of the homotypic and heterotypic cell junctions. Nectin-4 has been shown to be overexpressed in tumor cells and is believed to play a role in tumor cell growth and proliferation. High in normal embryonic and fetal tissue, Nectin-4 declines in adulthood, showing a limited distribution in healthy tissues. However, Nectin-4 is expressed on tumor cells in numerous cancer types including bladder, breast, gastric, lung and ovarian. In addition, we believe the favorable characteristics of BTC-targeted therapies may address some of the challenges in treating pancreatic cancer.

Our IND-enabling preclinical studies for BT8009 are currently ongoing.

Bicycle-Targeted Innate Immune Activators

Local activation of the innate immune system within tumors is a promising area for cancer drug discovery. Many of the current clinical programs require direct injection of molecules activating the innate immune system into tumors to avoid excessive systemic activation of the immune system and associated toxicity. Based on our experience with BTCs, we believe that *Bicycles* can systemically deliver activators of the innate immune system to tumors without activating the immune system in normal tissues. We believe that this approach has the potential to avoid the need for direct tumor injection and to allow inaccessible tumors to be reached, while enabling rapid systemic elimination of excess payloads in an inactive form.

Bicycle T-Cell Modulators

CD137

We are developing cytotoxic T-cell activators, designed to trigger an immune response to tumors. We have identified potent *Bicycle* activators of CD137, which is also known as 4-1BB, a tumor necrosis factor receptor, or TNFR, family member. We believe that *Bicycles* represent a differentiated approach to target CD137 that may confer several advantages over existing modalities due to the multivalency and PK characteristics of *Bicycles*. Our *Bicycle* T-cell modulators are designed to circumvent the limitations of antibody and biologic therapies, such as liver toxicity and limited efficacy, and to better enable combination therapy. We are also exploring CD137 in a bi-specific format linked to other *Bicycles* that bind tumor antigens, inhibit checkpoint proteins or otherwise activate the immune system.

Beyond Oncology

We have entered into several collaborations outside of our internal focus in oncology to leverage the broad applicability of *Bicycles*. Our strategic collaborations are based on the ability of *Bicycles* to address a wide variety of targets and we are working with collaborators with deep therapeutic expertise outside of oncology to enable us to more efficiently develop novel medicines for patients.

AstraZeneca. In November 2016, we entered into a research collaboration agreement with AstraZeneca AB, or AstraZeneca, with a focus on targets within respiratory, cardiovascular and metabolic disease.

Bioverativ. In August 2017, we entered into a collaboration agreement with Bioverativ, Inc., or Bioverativ, focused on non-malignant hematology indications, including hemophilia.

Dementia Discovery Fund. In May 2019, we entered into a collaboration with the Dementia Discovery Fund focused on dementia.

Oxurion. In August 2013, we entered into a research collaboration and license agreement with Oxurion NV (formerly ThromboGenics NV), or Oxurion, focused on ophthalmology. The lead molecule of the partnership is THR-149, a novel plasma kallikrein inhibitor, for the treatment of diabetic macular edema. A Phase I clinical trial of THR-149 is currently ongoing. The Phase I clinical trial, which is being conducted by Oxurion, is an open-label, multi-center, dose escalation trial to evaluate the safety of a single intravitreal injection of THR-149 of three dose levels for the treatment of diabetic macular edema, or DME, with a primary endpoint of dose-limiting toxicities up to the Day 14 visit. On April 24, 2019, we and Oxurion announced that enrollment in the trial had been completed, with 15 patients enrolled.

Our Strategy

Our mission is to become a leading biopharmaceutical company by pioneering *Bicycles* as a novel therapeutic modality to treat diseases that are inadequately addressed with existing treatment modalities. Specifically, we seek to execute on the following strategy to maximize the value of our novel technology and pipeline:

- ***Advance our lead product candidate, BT1718, through clinical development.*** BT1718 is being investigated in an ongoing Phase I/IIa clinical trial sponsored by CRUK. We expect to report preliminary data from the Phase I part of this clinical trial in the second half of 2019. We intend to advance development of this candidate aggressively across oncology indications in which the target MT1-MMP is expressed.

- ***Advance our other Bicycle Toxin Conjugate programs into clinical development.*** We intend to progress our IND-enabling activities for BT5528 and BT8009 to advance these programs into clinical development for oncology indications. Based on promising observations from our preclinical models, we believe EphA2 and Nectin-4 are attractive targets for cytotoxin delivery and that *Bicycles* provide a promising delivery modality.

- ***Pursue clinical development of our discovery programs.*** We intend to continue our ongoing discovery activities to screen and select promising candidates for oncology indications. For example, our discovery pipeline includes T-cell modulators, from which we expect to identify a development candidate. In addition, we are also developing *Bicycle*-targeted innate immune activators.

- ***Leverage our powerful proprietary screening platform and novel Bicycle modality to grow our pipeline.*** Our novel and proprietary phage display screening platform allows us to rapidly and efficiently identify potential candidates for development. We can incorporate a wide range of small molecule scaffolds into *Bicycles* to increase diversity and confer differentiated physicochemical and structural properties. We have used our powerful *Bicycle* screening platform to identify our current pipeline of promising BTCs, innate immune activators and T-cell modulators, and intend to use it to develop a broader pipeline of diverse product candidates.

- ***Collaborate strategically with leading organizations to access enabling technology and expertise in order to expand the application of our novel Bicycle modality to indications beyond oncology.*** We are collaborating with leading biopharmaceutical companies and organizations to apply our novel *Bicycle* modality to other disease areas, including neurological, anti-bacterial, cardiovascular, hematological, ophthalmological and respiratory indications. We may opportunistically enter into additional collaborations in the future to apply our technology to areas of unmet medical need.

- ***If approved, maximize the commercial potential of our product candidates by either establishing our own sales and marketing infrastructure or doing so through collaborations with others.*** Subject to receiving marketing approval, we intend to pursue the commercialization of our product candidates either by building internal sales and marketing capabilities or doing so through opportunistic collaborations with others.

Our Team

Our management team includes veterans in drug development with executive experience at leading pharmaceutical companies including GlaxoSmithKline, Novartis and Pfizer. Our board of directors and scientific advisory board include industry experts and seasoned investors, with extensive experience in immuno-oncology. We are supported by prominent healthcare-focused investment funds, including Ahren Innovation Capital, Atlas Venture Fund, Cambridge Innovation Capital, Longwood Fund, Novartis Venture Fund, S.R. One, Limited, SV Health Investors, Tybourne Capital (HK) Management Limited and Vertex HC Ventures.

Our Intellectual Property

We have generated substantial intellectual property, including three patent families directed to novel scaffolds, 11 patent families directed to Bicycle's platform technology, 63 patent families directed to bicyclic peptides and related conjugates, and six patent families directed to clinical indications and other properties of development assets. The work we have conducted in developing *Bicycles* and our proprietary screening platform have created substantial know-how that we believe provides us with a competitive advantage.

Corporate History

In 2009, we were incorporated as a limited liability company under the laws of England and Wales. In 2017, we effected a reorganization to create a new holding company which, in connection with this offering, will be re-registered as a public limited company named Bicycle Therapeutics plc., which will be the issuer of the securities described in this prospectus. Bicycle Therapeutics plc will be the parent company of three wholly owned subsidiaries, two of which are based in Cambridge, England and one of which has its principal office in Lexington, Massachusetts, near Boston, that will carry on our business.

The English subsidiaries are BicycleTx Limited and BicycleRD Limited, and the U.S. subsidiary is Bicycle Therapeutics Inc. Our principal executive offices are located at B900, Babraham Research Campus, Cambridge, CB22 3AT, United Kingdom, and our phone number is +44 1223 261503. Our website address is http://www.bicycletherapeutics.com. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus.

Share Capital Reorganization and Re-Registration

Prior to the consummation of this offering, Bicycle Therapeutics Limited will be re-registered as a public limited company and will change its name from Bicycle Therapeutics Limited to Bicycle

Therapeutics plc. Please see the "Share Capital Reorganization and Re-Registration" section for more information.

Risks Affecting Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth in the section titled "Risk Factors" before deciding whether to invest in our ADSs. Among these important risks are, but not limited to, the following:

- We have a history of significant operating losses and expect to incur significant and increasing losses for the foreseeable future, and we may never achieve or maintain profitability.
- Even if this offering is successful, we will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.
- Our product candidates and those of our collaborators will need to undergo preclinical and clinical trials that are time consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If preclinical or clinical trials of our or their product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA, the EMA and any other comparable regulatory authority, additional costs may be incurred or delays experienced in completing the development of these product candidates, or their development may be abandoned.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any collaborators, will obtain marketing approval to commercialize a product candidate.
- We are at a very early stage in our development efforts, our product candidates and those of our collaborators represent a new category of medicines and may be subject to heightened regulatory scrutiny until they are established as a therapeutic modality.
- We may not be successful in our efforts to identify or discover additional product candidates.
- We face significant competition and if our competitors develop and market products that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.
- As a company based outside of the United States, we are subject to economic, political, regulatory and other risks associated with international operations.
- For certain product candidates, we depend, or will depend, on development and commercialization collaborators to develop and conduct clinical trials, obtain regulatory approvals, and if approved, market and sell product candidates. If such collaborators fail to perform as expected, the potential for us to generate future revenue from such product candidates would be significantly reduced and our business would be harmed.
- If we are unable to obtain and maintain patent and other intellectual property protection for our products and product candidates, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and

commercialize products similar or identical to ours, and our ability to successfully commercialize our products and product candidates may be adversely affected.

- If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.
- Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.
- We do not know whether an active, liquid and orderly trading market will develop for our ADSs or what the market price of our ADSs will be. As a result, it may be difficult for you to sell your ADSs.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. For so long as we remain an emerging growth company, we are permitted and intend to rely on certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock. See "Management's Discussion and Analysis of Financial Condition and Results of Operations — Emerging Growth Company Status."

We will remain an emerging growth company until the earlier to occur of (1) the last day of 2023, (2) the last day of the fiscal year in which we have total annual gross revenues of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer," under the rules of the U.S. Securities and Exchange Commission, or SEC, which means the market value of our equity securities that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" if the market value of our ordinary shares held by non-affiliates is below $250 million (or $700 million if our annual revenue is less than $100 million) as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

The Offering

ADSs offered by us	4,333,333 ADSs, each ADS representing one ordinary share.
Ordinary shares outstanding immediately after this offering	17,696,417 ordinary shares (or 18,346,417 ordinary shares if the underwriters' option to purchase additional ADSs is exercised in full).
ADSs outstanding immediately after this offering	4,333,333 ADSs (or 4,983,333 ADSs if the underwriters' option to purchase additional ADSs is exercised in full).
Underwriters' option to purchase additional ADSs	We have granted a 30-day option to the underwriters to purchase up to an aggregate of 650,000 additional ADSs.
American Depositary Shares	Each ADS represents one ordinary share with a nominal value of £0.01 per ordinary share. You will have the rights of an ADS holder as provided in the deposit agreement among us, the depositary and all holders and beneficial owners of ADSs issued thereunder. To better understand the terms of the ADSs, you should carefully read the section in this prospectus titled "Description of American Depositary Shares." We also encourage you to read the deposit agreement, which is filed as an exhibit to the registration statement that includes this prospectus.
Depositary	Citibank, N.A.
Use of proceeds	We estimate that we will receive net proceeds from this offering of approximately $57.1 million, or $66.1 million, if the underwriters exercise their option to purchase additional ADSs in full, based upon an assumed initial public offering price of $15.00 per ADS, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We expect to use the net proceeds from this offering to (i) complete preparation for Phase II and III clinical development of BT1718 and to advance BT5528 and BT8009 through Phase I and IIa clinical development; (ii) advance our CD137 programs through preclinical development and to advance one CD137 multimeric program through Phase I clinical development; and (iii) the remainder on drug discovery, further expansion of our infrastructure to support our pipeline as well as to fund working capital and other general corporate purposes. See "Use of Proceeds" for additional information.
Risk factors	You should carefully read "Risk Factors" and the other information in this prospectus for a discussion of factors that you should consider before deciding to invest in the ADSs.

Proposed Nasdaq Global Market trading symbol "BCYC"

Certain of our existing shareholders and their affiliated entities, including those affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $25.0 million of ADSs in this offering at the initial public offering price per ADS and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no ADSs to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no ADSs in this offering.

The number of ordinary shares to be outstanding after this offering is based on 898,678 ordinary shares (which includes 56,643 unvested restricted shares subject to repurchase by us) outstanding as of March 31, 2019, and also gives effect to (i) the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares prior to the completion of this offering, and (iii) the automatic conversion of all outstanding convertible preferred shares, including those issuable upon exercise of the warrants referenced in (i) and (ii) above, into an aggregate of 12,464,406 ordinary shares upon the completion of this offering, and excludes:

- 930,861 ordinary shares issuable upon the exercise of options to subscribe for ordinary shares outstanding as of March 31, 2019 at a weighted average exercise price of $1.33 per ordinary share;
- 627,382 ordinary shares reserved for future issuance as of March 31, 2019 in connection with equity awards, which shares will no longer be reserved following this offering;
- 2,470,583 ordinary shares that will be made available for future issuance under our 2019 Share Option Plan upon the effectiveness of the registration statement of which this prospectus forms a part (from which we intend to grant options to purchase an aggregate of 1,311,061 ordinary shares to certain of our directors and officers upon the effectiveness of the registration of which this prospectus forms a part); and
- 215,000 ordinary shares that will be made available for future issuance under our 2019 Employee Share Purchase Plan, upon the effectiveness of the registration statement of which this prospectus forms a part.

Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

- the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares, the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares and the automatic conversion of all outstanding convertible preferred shares as of March 31, 2019, including those issuable upon exercise of the above-referenced warrants, into an aggregate of 12,464,406 ordinary shares upon the completion of this offering;
- the effectiveness of the share capital reorganization effective on May 13, 2019, which is intended to have the effect of a 1-for-1.429 forward share split of our ordinary share capital and corresponding adjustment in the conversion rate of our preferred shares into ordinary shares. See "Share Capital Reorganization and Re-Registration;"
- the effectiveness of our amended and restated memorandum and articles of association upon the closing of this offering;
- the reclassification of warrant liability into additional paid-in capital, upon the completion of this offering;
- no issuance or exercise of share options after March 31, 2019; and
- no exercise by the underwriters of their option to purchase up to an additional 650,000 ADSs in this offering.

Summary Consolidated Financial Data

The following tables present the summary consolidated financial data as of the dates and for the periods indicated for Bicycle Therapeutics Limited. We derived the summary consolidated statements of operations and comprehensive loss data for the years ended December 31, 2017 and 2018 and the consolidated balance sheet data as of December 31, 2018 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical audited consolidated financial statements as of December 31, 2017 have been restated. See Note 1 to the audited consolidated financial statements included elsewhere in this prospectus. The consolidated statements of operations data for the three months ended March 31, 2018 and 2019 and the consolidated balance sheet data as of March 31, 2019 have been derived from our unaudited consolidated financial statements included elsewhere in this prospectus and have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of the financial information contained in those statements. We prepare our consolidated financial statements in accordance with U.S. GAAP.

Our historical results are not necessarily indicative of our future results, and our operating results for the interim period ended March 31, 2019 are not necessarily indicative of the results that may be expected for the full year ending December 31, 2019 or any other interim periods or any future period. You should read this data together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information under the sections titled "Selected Consolidated Financial Data", "Capitalization" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

The functional currency of Bicycle Therapeutics Limited and its wholly owned subsidiaries in the United Kingdom, BicycleTx Limited and BicycleRD Limited, is the pound sterling. The functional currency of Bicycle Therapeutics Inc. is the U.S. dollar. For financial reporting purposes, the financial statements of Bicycle Therapeutics Limited, BicycleTx Limited and BicycleRD Limited, which are prepared using the functional currency, have been translated into U.S. dollars. Our assets and liabilities are translated at the exchange rates at the balance sheet date, our revenue and expenses are translated at average exchange rates and shareholders' (deficit) equity is translated based on historical exchange rates. Translation adjustments are not included in determining net loss but are included in foreign exchange translation adjustment within accumulated other comprehensive income (loss), a component of shareholders' (deficit) equity.

Foreign currency transactions in currencies different from the functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss.

As of March 29, 2019, the last business day of the three months ended March 31, 2019, the representative exchange rate was $1.3032 = £1.00.

Prior to the completion of this offering, we intend to reorganize our share capital and to re-register as a public limited company and change our name from Bicycle Therapeutics Limited to Bicycle Therapeutics plc. See "Share Capital Reorganization and Re-Registration".

	Year ended December 31,		Three months ended March 31,	
	2017	2018	2018	2019
	(as restated)	(in thousands, except share and per share data)		
Statement of Operations Data:				
Collaboration revenues	$ 2,060	$ 7,136	$ 2,808	$ 6,384
Operating expenses:				
Research and development	11,866	20,761	3,709	6,276
General and administrative	6,407	8,121	1,988	3,402
Total operating expenses	18,273	28,882	5,697	9,678
Loss from operations	(16,213)	(21,746)	(2,889)	(3,294)
Other income (expenses):				
Interest and other income (expense)	50	169	(3)	64
Other expense, net	(119)	(665)	(38)	(3,193)
Total other expense, net	(69)	(496)	(41)	(3,129)
Net loss before income tax provision	(16,282)	(22,242)	(2,930)	(6,423)
Provision for (benefit from) income taxes	(23)	(396)	(396)	80
Net loss	$ (16,259)	$ (21,846)	$ (2,534)	$ (6,503)
Net loss attributable to ordinary shareholders	$ (16,259)	$ (21,846)	$ (2,534)	$ (6,503)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (48.81)	$ (49.78)	$ (6.38)	$ (7.80)
Weighted average ordinary shares outstanding, basic and diluted	333,125	438,862	397,483	834,043
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted (unaudited)		$ (1.93)		$ (0.25)
Pro forma weighted average number of ordinary shares outstanding, basic and diluted (unaudited)		10,954,310		13,293,400

See Note 2 within the notes to our consolidated financial statements appearing at the end of this prospectus for a description of the method used to calculate basic and diluted net loss per share applicable to ordinary shareholders and unaudited pro forma basic and diluted net loss per

share, as adjusted to reflect the impact of the share capital reorganization and issuance of bonus shares (Note 1).

	As of March 31, 2019		
	Actual	Pro forma[1]	Pro forma as adjusted[2]
	(in thousands)		
Balance Sheet Data:			
Cash	$ 59,364	$ 59,371	$ 116,451
Working capital[3]	61,500	61,507	118,587
Total assets	77,794	77,801	134,881
Total deferred revenue	9,604	9,604	9,604
Warrant liability	8,101	—	—
Convertible preferred shares	123,780	—	—
Total shareholders' (deficit) equity	$ (74,973)	$ 56,915	$ 113,995

(1) The unaudited pro forma balance sheet data gives effect to (i) the exercise of warrants to subscribe for 200,000 Series A preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 preferred shares immediately prior to the completion of this offering, (iii) the automatic conversion of all outstanding convertible preferred shares as of March 31, 2019, including those referenced in (i) and (ii) above, into an aggregate of 12,464,406 ordinary shares upon completion of this offering, and (iv) the reclassification of warrant liability into additional paid-in capital, upon the completion of this offering.

(2) The pro forma as adjusted balance sheet data give further effect to our issuance and sale of 4,333,333 ADSs in this offering at an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, working capital, total assets and total shareholders' (deficit) equity by $4.0 million, assuming that the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same. Each increase (decrease) of 1,000,000 in the number of ADSs offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, total assets and total shareholders' (deficit) equity by $14.0 million, assuming no change in the initial public offering price per ADS.

(3) We define working capital as current assets less current liabilities.

RISK FACTORS

Investing in our ADSs involves a high degree of risk. Before deciding whether to invest, you should carefully consider the following risks and uncertainties, together with all other information in this prospectus, including our consolidated financial statements and related notes and "Management's Discussion and Analysis of Results of Operations and Financial Condition" before investing in our ADSs. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and/or growth prospects. In such an event, the market price of our ADSs could decline and you may lose all or part of your investment. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our ADSs could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our ADSs. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Special Note Regarding Forward-Looking Statements" in this prospectus.

Risks Related to Our Financial Position and Need for Additional Capital

We have a history of significant operating losses and expect to incur significant and increasing losses for the foreseeable future, and we may never achieve or maintain profitability.

We do not expect to generate revenue or profitability that is necessary to finance our operations in the short term. We incurred net losses of $16.3 million and $21.8 million for the years ended December 31, 2017 and 2018, respectively, and $2.5 million and $6.5 million, for the three months ended March 31, 2018 and 2019, respectively. In addition, our accumulated deficit as of December 31, 2018 and March 31, 2019 was $69.9 million and $76.4 million, respectively. To date, we have not commercialized any products or generated any revenues from the sale of products, and absent the realization of sufficient revenues from product sales, we may never attain profitability in the future. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders' (deficit) equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials with respect to our lead product candidate, BT1718, and our other product candidates in our *Bicycle* Toxin Conjugate, or BTC, program;
- initiate and continue research, preclinical and clinical development efforts for any future product candidates;
- seek to discover and develop additional product candidates and further expand our clinical product pipeline;
- seek marketing and regulatory approvals for any product candidates that successfully complete clinical trials;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- expand our research and development infrastructure, including hiring and retaining additional personnel, such as clinical, quality control and scientific personnel;

- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize products for which we obtain marketing approval, if any;
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development.

Our ability to become and remain profitable depends on our ability to generate revenue. Generating product revenue will depend on our or any of our collaborators' ability to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. Successful commercialization will require achievement of key milestones, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, and if or when we might achieve profitability. We and any collaborators may never succeed in these activities and, even if we do, or any collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our revenue to date has been primarily generated from our research collaborations with AstraZeneca AB, or AstraZeneca, Bioverativ, Inc., or Bioverativ, and Oxurion NV (formerly ThromboGenics NV), or Oxurion. There can be no assurance that we will generate revenue from these collaborations in the future.

Our failure to become and remain profitable would depress the market price of our ADSs and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to suffer losses, investors may not receive any return on their investment and may lose their entire investment.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Our business commenced operations in 2009. Our operations to date have been limited to financing and staffing our company, developing our technology, conducting preclinical research and early-stage clinical trials for our product candidates and pursuing strategic collaborations to advance our product candidates. We have not yet demonstrated an ability to successfully conduct late-stage clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they would be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Even if this offering is successful, we will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. For example, in the years ended December 31, 2017 and 2018, we used $1.4 million and $26.1 million, respectively, in net cash for our operating activities, and in the three months ended March 31, 2018 and 2019, we used $7.3 million and $5.2 million, respectively, in net cash for our operating activities, substantially all of which related to research and development activities. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and preclinical development efforts for and seek marketing approval for, our current product candidates or any future product candidates. In addition, if we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a collaborator. Furthermore, following the completion of this offering, we expect to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We plan to use the net proceeds of this offering primarily to complete preparation for Phase II and III clinical development of BT1718 and to advance BT5528 and BT8009 through Phase I clinical development and complete preparations for Phase II development activities, advance our CD137 programs through preclinical development and to advance at least one CD137 multimeric program through Phase I clinical development, and the remainder on drug discovery, further expansion of our infrastructure to support our pipeline as well as to fund working capital and other general corporate purposes. We will be required to expend significant funds in order to advance the development of the product candidates in our pipeline, as well as other product candidates we may seek to develop. In addition, while we may seek one or more collaborators for future development of our product candidates, we may not be able to enter into a collaboration for any of our product candidates for such indications on suitable terms, on a timely basis or at all. In any event, the net proceeds of this offering and our existing cash will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that the net proceeds from this offering, together with our existing cash of $59.4 million as of March 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements for at least the next twelve months. Our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds

sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, our current and future product candidates;
- our ability to enter into, and the terms and timing of, any collaborations, licensing or other arrangements;
- our ability to identify one or more future product candidates for our pipeline;
- the number of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights including enforcing and defending intellectual property related claims; and
- the costs of operating as a public company.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or cause us to relinquish valuable rights.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances, licensing arrangements or monetization transactions. To the extent that we raise additional capital through the sale of equity, convertible debt securities or other equity-based derivative securities, your ownership interest will be diluted and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. Any indebtedness we incur would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our ADSs to decline and existing shareholders may not agree with our financing plans or the terms of such financings. If we raise additional funds through strategic partnerships and alliances, licensing arrangements or monetization transactions with third parties, we may have to relinquish valuable rights to our technologies, or our product candidates, or grant licenses on terms unfavorable to us. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates

We are substantially dependent on the success of our internal development programs and of our product candidates from our BTC program which may not successfully complete clinical trials, receive regulatory approval or be successfully commercialized.

Our future success will depend heavily on the success of our internal development programs and of product candidates from our BTC program.

Within our BTC program, we are investigating BT1718 for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial in collaboration with the Centre for Drug Development of Cancer Research UK, or CRUK. Upon the completion of the Phase I/IIa clinical trial for BT1718, we have the right to obtain a license to the results of the clinical trial from CRUK upon the payment of a milestone, in cash and ordinary shares with a combined value in a mid six digit dollar amount. If we do not exercise our right to obtain a license to the results of the clinical trial or we fail to obtain a license, our ability to continue development of BT1718 would be negatively impacted. BT1718 is designed to target tumors that express MT1-MMP. We are also developing BT5528 and BT8009, which are BTCs targeting Ephrin type-A receptor 2, or EphA2, and Nectin-4, respectively, for oncology indications. These target proteins have an established role in cell invasion and metastasis and are overexpressed in many solid tumors, but there can be no assurance our BTCs will ever demonstrate evidence of safety or effectiveness for any use or receive U.S. or E.U. regulatory approval in any indication. Even if clinical trials show positive results, there can be no assurance that the FDA in the U.S., EMA in Europe or similar regulatory authorities will approve our BTCs or any of our other product candidates for any given indication for several potential reasons, including the failure to follow Good Clinical Practice, or GCP, a negative assessment of the risks and benefits, insufficient product quality control and standardization, failure to have Good Manufacturing Practices, or GMP, compliant manufacturing facilities, or the failure to agree with regulatory authorities on clinical endpoints.

Our ability to successfully commercialize our BTCs and our other product candidates will depend on, among other things, our ability to:

- successfully complete preclinical studies and clinical trials;
- receive regulatory approvals from the FDA, the EMA and other similar regulatory authorities;
- establish and maintain collaborations with third parties for the development and/or commercialization of our product candidates, or otherwise build and maintain strong development, sales, distribution and marketing capabilities that are sufficient to develop products and launch commercial sales of any approved products;
- obtain coverage and adequate reimbursement from payors such as government health care systems and insurance companies and achieve commercially attractive levels of pricing;
- secure acceptance of our product candidates from physicians, health care payors, patients and the medical community;
- produce, through a validated process, in manufacturing facilities inspected and approved by regulatory authorities, including the FDA, sufficiently large quantities of our product candidates to permit successful commercialization;
- manage our spending as expenses increase due to clinical trials and commercialization; and
- obtain and enforce sufficient intellectual property rights for any approved products and product candidates.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a new drug application, or NDA, to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market our product candidates, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that our product candidates will be successfully developed or commercialized. If we are unable to develop, or obtain regulatory approval for, or, if approved, to successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business.

We are at a very early stage in our development efforts, our product candidates and those of our collaborators represent a new category of medicines and may be subject to heightened regulatory scrutiny until they are established as a therapeutic modality.

Bicycles represent a new therapeutic modality of peptide compounds intended to combine targeting abilities of antibodies with performance of small molecules. Our product candidates may not demonstrate in patients any or all of the pharmacological benefits we believe they may possess. We have not yet succeeded and may never succeed in demonstrating efficacy and safety for these or any other product candidates in clinical trials or in obtaining marketing approval thereafter.

Regulatory authorities do not have experience with *Bicycles* and may require evidence of safety and efficacy that goes beyond what we and our collaborators have included in our development plans. In such a case, development of *Bicycle* product candidates may be more costly or time-consuming than expected, and our candidate products and those of our collaboration partners may not prove to be viable.

If we are unsuccessful in our development efforts, we may not be able to advance the development of our product candidates, commercialize products, raise capital, expand our business or continue our operations.

Our product candidates and those of our collaborators will need to undergo preclinical and clinical trials that are time consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If preclinical or clinical trials of our or their product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA, the EMA and any other comparable regulatory authority, additional costs may be incurred or delays experienced in completing, the development of these product candidates, or their development may be abandoned.

The FDA in the United States, the EMA in the European Union and the European Economic Area, and any other comparable regulatory authorities in other jurisdictions must approve new product candidates before they can be marketed, promoted or sold in those territories. We have not previously submitted an IND or NDA to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. We must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that our product candidates are safe and effective for a specific indication before they can be approved for commercial distribution. We cannot be certain that our clinical trials for our product candidates will be successful or that any of our other product candidates will receive approval from the FDA, the EMA or any other comparable regulatory authority.

Preclinical studies and clinical trials are long, expensive and unpredictable processes that can be subject to extensive delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. It may take several years and require significant

expenditures to complete the preclinical studies and clinical trials necessary to commercialize a product candidate, and delays or failure are inherently unpredictable and can occur at any stage. We may also be required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we contemplate, which may lead to us incurring additional unplanned costs or result in delays in clinical development. In addition, we may be required to redesign or otherwise modify our plans with respect to an ongoing or planned clinical trial, and changing the design of a clinical trial can be expensive and time consuming. An unfavorable outcome in one or more trials would be a major setback for our product candidates and for us. An unfavorable outcome in one or more trials may require us to delay, reduce the scope of or eliminate one or more product development programs, which could have a material adverse effect on our business, financial position, results of operations and future growth prospects.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval for our product candidates. The FDA, EMA or any other comparable regulatory authority may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

In connection with clinical trials of our product candidates, we face a number of risks, including risks that:

- a product candidate is ineffective or inferior to existing approved products for the same indications;
- a product candidate causes or is associated with unacceptable toxicity or has unacceptable side effects;
- patients may die or suffer adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results may not confirm the positive results of earlier trials;
- the results may not meet the level of statistical significance required by the FDA, the EMA or other relevant regulatory agencies to establish the safety and efficacy of our product candidates for continued trial or marketing approval; and
- our collaborators may be unable or unwilling to perform under their contracts.

Furthermore, we sometimes estimate for planning purposes the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, the receipt of marketing approval or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions, which may cause the timing of achievement of the milestones to vary considerably from our estimates. If we fail to achieve milestones in the timeframes we expect, the commercialization of our product candidates may be delayed, we may not be entitled to receive certain contractual payments, which could have a material adverse effect on our business, financial position, results of operations and future growth prospects.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate as well as the completion of required follow-up periods. Patients may be unwilling to participate in our clinical trials because of negative publicity from adverse events related to novel therapeutic approaches, competitive clinical trials for similar patient populations, the existence of current treatments or for other reasons. Enrollment risks are heightened with respect to certain indications that we may target for one or more of our product candidates that may be rare diseases, which may limit the pool of patients that may be enrolled in our planned clinical trials. The timeline for recruiting patients, conducting trials and obtaining regulatory approval of our product candidates may be delayed, which could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with the required or desired characteristics, to complete our clinical trials in a timely manner. For example, due to the nature of the indications that we are initially targeting, patients with advanced disease progression may not be suitable candidates for treatment with our product candidates and may be ineligible for enrollment in our clinical trials. Therefore, early diagnosis in patients with our target diseases is critical to our success. Patient enrollment and trial completion is affected by factors including the:

- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- eligibility and exclusion criteria;
- safety profile, to date, of the product candidate under study;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of our approach to treatment of diseases;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- degree of progression of the subject's disease at the time of enrollment;
- proximity and availability of clinical trial sites for prospective subjects;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

In addition, clinical testing of BT1718 is currently taking place outside of the U.S. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with academic partners or contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;

- the absence in some countries of established groups with sufficient regulatory expertise for review of protocols related to our novel approach;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in the results of completed clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. For example, the Phase I/IIa trial of BT1718 is being conducted by CRUK at up to six sites in the United Kingdom, and the findings may not be replicated in future trials at global clinical trial sites in a later stage clinical trial conducted by us or our collaborators. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval.

Preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics could harm our drug development strategy.

We may employ companion diagnostics to help us more accurately identify patients within a particular subset, both during our clinical trials and in connection with the commercialization of our product candidates that we are developing or may in the future develop. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate regulatory approval prior to commercialization. We do not develop companion diagnostics internally and thus we will be dependent on the sustained cooperation and

effort of our third-party collaborators in developing and obtaining approval for these companion diagnostics. There can be no guarantees that we will successfully find a suitable collaborator to develop companion diagnostics. We and our collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, our collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community. If such companion diagnostics fail to gain market acceptance, our ability to derive revenues from sales of any products, if approved, will be adversely affected. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

Our current or future product candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could halt their clinical development, prevent their marketing approval, limit their commercial potential or result in significant negative consequences.

Undesirable or clinically unmanageable side effects could occur and cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. To date, subjects exposed to BT1718 in the ongoing Phase I/IIa clinical trial have experienced drug-related side effects including fatigue, liver function abnormalities and muscle pain.

If unacceptable side effects arise in the development of our product candidates, we, the FDA or comparable foreign regulatory authorities, the Institutional Review Boards, or IRBs, or independent ethics committees at the institutions in which our studies are conducted, or the Data Safety Monitoring Board, or DSMB, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial, or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We may be required to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

Our product candidates are currently undergoing safety testing in the form of Phase I/IIa clinical trials. None of our products have completed this testing to date. While our current and future product candidates will undergo safety testing to the extent possible and, where applicable, under such conditions discussed with regulatory authorities, not all adverse effects of drugs can be

predicted or anticipated. Unforeseen side effects could arise either during clinical development or, if such side effects are more rare, after our products have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. So far, we have not demonstrated, and we cannot predict if ongoing or future clinical trials will demonstrate, that BT1718 or any other of our product candidates are safe in humans.

Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following consequences could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any collaborators, may need to recall the product, or be required to change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning or a contraindication;
- we, or any collaborators, may be required to create a medication guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

If any of our current or future product candidates fail to demonstrate safety and efficacy in clinical trials or do not gain marketing approval, we will not be able to generate revenue and our business will be harmed. Any of these events could harm our business and operations, and could negatively impact the price of our ADSs.

We may not be successful in our efforts to identify or discover additional product candidates.

Although we intend to utilize our *Bicycle* screening platform to explore other therapeutic opportunities in addition to the product candidates that we are currently developing, we may fail to identify other product candidates for clinical development for a number of reasons. For example, our research methodology may not be successful in identifying potential product candidates or those we identify may be shown to have harmful side effects or other characteristics that make them unmarketable or unlikely to receive regulatory approval. A key part of our strategy is to utilize our screening technology to identify product candidates to pursue in clinical development. Such product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development. If we fail to identify and develop additional potential product candidates, we may be unable to grow our business and our results of operations could be materially harmed.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- the impairment of our business reputation;
- the withdrawal of clinical trial participants;
- substantial monetary awards to patients or other claimants;
- costs due to related litigation;
- the distraction of management's attention from our primary business;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We believe our product liability insurance coverage is sufficient in light of our current commercial and clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage each time we commercialize an additional product; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our ADS price to decline and, if

judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Patients with the diseases targeted by certain of our product candidates, such as our lead indications in oncology, are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

We may seek designations for our product candidates with the FDA and other comparable regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, but there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and other comparable regulatory authorities offer certain designations for product candidates that are intended to encourage the research and development of pharmaceutical products addressing conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. There can be no assurance that we will successfully obtain such designation for any of our other product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Breakthrough Therapy Designation for one or more of our product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, if preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA are also eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of

our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

We may also seek Fast Track Designation for some of our product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track Designation does not provide assurance of ultimate FDA approval. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, in particular if such product candidate has received a Breakthrough Therapy Designation, the FDA may decide not to grant it. Moreover, a priority review designation does not result in expedited development and does not necessarily result in expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not mean that we will be successful in obtaining marketing approval of our current and future product candidates in other jurisdictions.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction, while a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. We do not have experience in obtaining reimbursement or pricing approvals in international markets.

Obtaining marketing approvals and compliance with regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our

products in certain countries outside of the United Kingdom and the United States. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

Risks Related to Commercialization of Our Product Candidates and Other Regulatory Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any collaborators, will obtain marketing approval to commercialize a product candidate.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends

non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or other regulatory authority. The FDA or other regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or other regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, regulatory agencies may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. Regulators may approve a product candidate for a smaller patient population, a different drug formulation or a different manufacturing process, than we are seeking. If we are unable to obtain necessary regulatory approvals, or more limited regulatory approvals than we expect, our business, prospects, financial condition and results of operations may suffer.

Any delay in obtaining or failure to obtain required approvals could negatively impact our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact the price of our ADSs.

We currently have no marketing, sales or distribution infrastructure with respect to our product candidates. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates.

We currently have no marketing, sales or distribution capabilities and have limited sales or marketing experience within our organization. If one or more of our product candidates is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize that product candidate, or to outsource this function to a third party. There are risks involved with either establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services.

Recruiting and training an internal commercial organization is expensive and time consuming and could delay any product launch. Some or all of these costs may be incurred in advance of any approval of any of our product candidates. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States or other target market that is sufficient in size or has adequate expertise in the medical markets that we intend to target.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- the inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product that we may develop;
- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates.

The market opportunities for any current or future product candidate we develop, if and when approved, may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed, and may be small.

Cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, surgery, radiation therapy, immunotherapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. We may initially seek approval of BT1718 and any other product candidates we develop as a therapy for patients who have received one or more prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first-line therapy, but there is no guarantee that product candidates we develop, even if approved, would be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

The number of patients who have the cancers we are targeting may turn out to be lower than expected. Additionally, the potentially addressable patient population for our current programs or future product candidates may be limited, if and when approved. Even if we obtain significant market share for any product candidate, if and when approved, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications, including use as first- or second-line therapy.

Even if we receive marketing approval of a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products, if approved.

Any marketing approvals that we receive for any current or future product candidate may be subject to limitations on the approved indicated uses for which the product may be marketed or the

conditions of approval, or contain requirements for potentially costly post-market testing and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval of any product candidate, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If the FDA or a comparable foreign regulatory authority approves a product candidate, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import and export and record keeping for the product candidate will be subject to extensive and ongoing regulatory requirements. These requirements include, among others, prohibitions on the promotion of an approved product for uses not included in the product's approved labeling, submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practice, or cGMP, and Good Clinical Practice, or GCP, for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with any approved candidate, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the labeling, distribution, marketing or manufacturing of the product, withdrawal of the product from the market, or product recalls;
- untitled and warning letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications we filed or suspension or revocation of license approvals;
- requirements to conduct post-marketing studies or clinical trials;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- product seizure or detention, or refusal to permit the import or export of the product; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval of a product. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We face significant competition and if our competitors develop and market products that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.

The life sciences industry is highly competitive. We are currently developing therapeutics that will compete, if approved, with other products and therapies that currently exist, are being developed or will in the future be developed, some of which we may not currently be aware.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities and other research institutions. Many of our competitors

have significantly greater financial, manufacturing, marketing, product development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing approval or discovering, developing and commercializing products in our field before we do.

There is a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. These treatments consist both of small molecule drug products, such as traditional chemotherapy, as well as novel immunotherapies. For example, a number of multinational companies as well as large biotechnology companies, including Astellas Pharma Inc., Seattle Genetics, Inc., AstraZeneca, and GlaxoSmithKline plc, are developing programs for the targets that we are exploring for our BTC programs. Furthermore, Agenus Inc., Bristol-Myers Squibb Company, Pfizer Inc., Roche Holding AG, or Roche, have or are developing programs for CD137, and Amgen Inc., Pieris Pharmaceuticals, Inc. and Roche are developing bi-specifics.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain FDA, EMA or other marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if the product candidate we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness.

Smaller and other early stage companies may also prove to be significant competitors. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. In addition, the biopharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our product candidates obsolete, less competitive or not economical.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, payors and others in the medical community.

We have never commercialized a product, and even if we obtain any regulatory approval for our product candidates, the commercial success of our product candidates will depend in part on the medical community, patients, and payors accepting products based on our *Bicycle* peptides in general, and our product candidates in particular, as effective, safe and cost-effective. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors and others in the medical community. Physicians are often reluctant to switch their patients from existing

therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

The degree of market acceptance of these product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the potential efficacy and potential advantages over alternative treatments;
- the frequency and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the frequency and severity of any side effects resulting from follow-up requirements for the administration of our product candidates;
- the relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and adequate reimbursement.

Even if a product candidate displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product, if approved for commercial sale, will not be known until after it is launched. Our efforts to educate the medical community and payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors, particularly due to the novelty of our *Bicycle* approach. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable.

If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.

We currently focus our research and product development on treatments for oncology indications and our product candidates are designed to target specific tumor antigens. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. Patient identification efforts also influence the ability to address a patient population. If efforts in patient identification are unsuccessful or less impactful than anticipated, we may not address the entirety of the opportunity we are seeking.

In addition, the tumor antigens that our product candidates target may not be expressed as broadly as we anticipate. Further, if companion diagnostics are not developed alongside our product candidates, testing patients for the tumor antigens may not be possible, which would hamper our ability to identify patients who could benefit from treatment with our product candidates.

As a result, the number of patients we are able to identify in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to access, all of which would adversely affect our business, financial condition, results of operations and prospects.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for any of our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

We expect the cost of our product candidates to be substantial, when and if they achieve market approval. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by private payors, such as private health coverage insurers, health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health care programs, such as Medicare and Medicaid. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize our product candidates, even if approved. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as the CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to coverage and reimbursement for novel products such as ours, as there is no body of established practices and precedents for these new products. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is: (1) a covered benefit under its health plan; (2) safe, effective and medically necessary; (3) appropriate for the specific patient; (4) cost-effective; and (5) neither experimental nor investigational. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Because our product candidates may have a higher cost of goods than conventional therapies, and may require long-term follow-up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. There is significant uncertainty related to insurance

coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

Outside the United States, certain countries, including a number of member states of the European Union, set prices and reimbursement for pharmaceutical products, or medicinal products, as they are commonly referred to in the European Union. These countries have broad discretion in setting prices and we cannot be sure that such prices and reimbursement will be acceptable to us or our collaborators. If the regulatory authorities in these jurisdictions set prices or reimbursement levels that are not commercially attractive for us or our collaborators, our revenues from sales by us or our collaborators, and the potential profitability of our drug products, in those countries would be negatively affected. An increasing number of countries are taking initiatives to attempt to reduce large budget deficits by focusing cost-cutting efforts on pharmaceuticals for their state-run health care systems. These international price control efforts have impacted all regions of the world, but have been most drastic in the European Union. Additionally, some countries require approval of the sale price of a product before it can be lawfully marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we, or any collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. As a result, we might obtain marketing approval for a product in a particular country, but then may experience delays in the reimbursement approval of our product or be subject to price regulations that would delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country.

Moreover, efforts by governments and payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate reimbursement for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our product candidates that receive marketing approval, or such authorities do not grant such products appropriate periods of data exclusivity before approving generic versions of such products, the sales of such products could be adversely affected.

Once a NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning, in part, that it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product, and the price of the branded product may be lowered.

The FDA may not accept for review or approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. It is unclear whether the FDA will treat the active ingredients in our product candidates as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for our products in the Orange Book. Three year exclusivity is given to a non-NCE drug if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the NDA. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws health information privacy and security laws, and other health care laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and

regulations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, or Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. "Remuneration" has been interpreted broadly to include anything of value. A person or entity does not need to have actual knowledge of the Anti-Kickback Statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA, or federal civil money penalties. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;

- the federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA, which impose criminal and civil penalties against individuals or entities for, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; knowingly making, using or causing to be made or used, a false statement of record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;

- the beneficiary inducement provisions of the CMP Law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the Anti-Kickback Statute, a person or entity does not need to have actual

knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, which impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their respective business associates, individuals and entities that perform services on their behalf that involve the use or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information;

- the U.S. federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payer. Many U.S. states have adopted laws similar to the Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our current and future business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will

involve substantial costs. If our operations, including our arrangements with physicians and other healthcare providers, some of whom receive stock options as compensation for services provided, are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs (such as Medicare and Medicaid), additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

Healthcare legislative reform measures and constraints on national budget social security systems may have a material adverse effect on our business and results of operations.

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as those we are developing. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in the United States, the ACA was enacted in 2010 which, among other things, subjects biologic products to potential competition by lower-cost biosimilars; addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increases the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extends the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjects manufacturers to new annual fees and taxes for certain branded prescription drugs; and provides incentives to programs that increase the federal government's comparative effectiveness research.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the current administration to repeal or replace certain aspects of the ACA. Further, since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provision of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. In addition, CMS recently issued a final rule that will give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

Concurrently, Congress has considered legislation that would repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or TCJA, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the

annual fee imposed on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device exercise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." More recently, in July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Congress also could consider additional legislation to repeal or replace other elements of the ACA. Thus, the full impact of the ACA, any law repealing or replacing elements of it, and the political uncertainty surrounding any repeal or replacement legislation on our business remains unclear.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.5 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and due to subsequent legislative amendments, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the current administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. For example, in November 2018, CMS issued a proposed rule for comment that would, among other things, provide Medicare prescription drug plans under Part D more transparency in pricing and greater flexibility to negotiate discounts for, and in certain circumstances exclude, drugs in the six "protected" formulary classes and allow Medicare Advantage plans to use certain drug management tools such as step therapy for physician-administered drugs. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

Additionally, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program.

There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of these governments and other payors to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any denial in coverage or reduction in reimbursement from Medicare or other government programs may result in a similar denial or reduction in payments from private payors, which may adversely affect our future profitability.

We are subject to the U.K. Bribery Act 2010, or the Bribery Act, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.

Our operations are subject to anti-corruption laws, including the Bribery Act, the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense. We and our commercial partners operate in a number of jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have

an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our activities in the United States subject us to various laws relating to foreign investment and the export of certain technologies, and our failure to comply with these laws or adequately monitor the compliance of our suppliers and others we do business with could subject us to substantial fines, penalties and even injunctions, the imposition of which on us could have a material adverse effect on the success of our business.

Because we have a U.S. subsidiary and substantial operations in the United States, we are subject to U.S. laws that regulate foreign investments in U.S. businesses and access by foreign persons to technology developed and produced in the United States. These laws include section 721 of the Defense Production Act of 1950, as amended by the Foreign Investment Risk Review Modernization Act of 2018, and the regulations at 31 C.F.R. Parts 800 and 801, as amended, administered by the Committee on Foreign Investment in the United States; and the Export Control Reform Act of 2018, which is being implemented in part through Commerce Department rulemakings to impose new export control restrictions on "emerging and foundational technologies" yet to be fully identified. Application of these laws, including as they are implemented through regulations being developed, may negatively impact our business in various ways, including by restricting our access to capital and markets; limiting the collaborations we may pursue; regulating the export our products, services, and technology from the United States and abroad; increasing our costs and the time necessary to obtain required authorizations and to ensure compliance; and threatening monetary fines and other penalties if we do not.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and

regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Our International Operations

As a company based outside of the United States, we are subject to economic, political, regulatory and other risks associated with international operations.

As a company based in the United Kingdom, our business is subject to risks associated with conducting business outside of the United States. Many of our suppliers and clinical trial relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements for product approvals;
- differing jurisdictions could present different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates of the pound sterling, U.S. dollar, euro and currency controls;
- changes in a specific country's or region's political or economic environment, including the implications of the recent decision of the United Kingdom to withdraw from the European Union;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- differing reimbursement regimes and price controls in certain non-U.S. markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad, including, for example, the variable tax treatment in different jurisdictions of options granted under our share option schemes or equity incentive plans;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- litigation or administrative actions resulting from claims against us by current or former employees or consultants individually or as part of class actions, including claims of wrongful terminations, discrimination, misclassification or other violations of labor law or other alleged conduct;
- difficulties associated with staffing and managing international operations, including differing labor relations;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

European data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information.

The collection and use of personal health data in the European Union is was governed by the provisions of the Data Protection Directive, and which, as of May 25, 2018, has been superseded by the GDPR. These directives impose several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The Data Protection Directive and GDPR also impose strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. While the Data Protection Directive did not apply to organizations based outside the EU, the GDPR has expanded its reach to include any business, regardless of its location, that provides goods or services to residents in the EU. This expansion would incorporate any potential clinical trial activities in EU member states. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for "sensitive information" which includes health and genetic information of data subjects residing in the EU. GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the European Union to the United States or other regions that have not been deemed to offer "adequate" privacy protections. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States, which may deviate slightly from the GDPR, may result in fines of up to 4% of global revenues, or € 20,000,000, whichever is greater. As a result of the implementation of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ADSs.

On June 23, 2016, the U.K. held a referendum in which a majority of the eligible members of the electorate voted for the U.K. to leave the European Union. The U.K's withdrawal from the European Union is commonly referred to as Brexit. Pursuant to Article 50 of the Treaty on European Union, the U.K. will cease to be a EU Member State either on the effective date of a withdrawal agreement (entry into such a withdrawal agreement will require U.K. parliamentary approval) or, failing that, two years following the U.K.'s notification of its intention to leave the European Union (the Brexit Date), unless the European Council (together with the U.K.) unanimously decides to extend the two year period. On March 29, 2017, the U.K. formally notified the European Council of its intention to leave the European Union. It is unclear how long it will take to negotiate a withdrawal agreement, but it appears likely that Brexit will continue to involve a process of lengthy negotiations between the U.K. and EU Member States to determine the future terms of the U.K's relationship with the European Union. For example, in March 2018, the U.K. reached a provisional agreement (the "Withdrawal Agreement") with the European Union on transitional arrangements following the

U.K's exit (which are intended to enable the U.K. to remain within the European Union single market and customs union for a transitional period through 2020), but this Withdrawal Agreement needs to be formally agreed as part of the withdrawal arrangements currently under negotiation. Given that no formal withdrawal arrangements have been agreed, there have been several extensions to the Brexit Date and the U.K. has yet to formally leave the European Union. On April 11, 2019, the European Union granted the U.K. a further extension to the Brexit Date until October 31, 2019. The purpose of this extension is to allow for the ratification of the Withdrawal Agreement by the U.K. House of Commons. If the Withdrawal Agreement is ratified, the U.K. will leave the European Union earlier than October 31, 2019. As a condition of the extension, the U.K. must take part in European Union elections on May 23, 2019. If it does not, the U.K. must leave the European Union on June 1, 2019 without any formal withdrawal arrangements.

These developments have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in the United Kingdom and Europe. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the market price of our ADSs. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which European Union rules and regulations to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. If the United Kingdom and the European Union are unable to negotiate acceptable withdrawal terms or if other EU Member States pursue withdrawal, barrier-free access between the United Kingdom and other EU Member States or among the EEA overall could be diminished or eliminated.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers that could make our doing business in Europe more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Furthermore, at present, there are no indications of the effect Brexit will have on the pathway to obtaining marketing approval for any of our product candidates in the United Kingdom, or what, if any, role the EMA may have in the approval process.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, may adversely affect us. Although we are based in the United Kingdom, we source research and development, manufacturing, consulting and other services from the United States and the European Union. Further, potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the price of our ADSs may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the euro, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

Risks Related to Our Dependence on Third Parties

For certain product candidates, we depend, or will depend, on development and commercialization collaborators to develop and conduct clinical trials with, obtain regulatory approvals for, and if approved, market and sell product candidates. If such collaborators fail to perform as expected, the potential for us to generate future revenue from such product candidates would be significantly reduced and our business would be harmed.

For certain products candidates, we depend, or will depend, on our development and commercial collaborators to develop, conduct clinical trials of, and, if approved, commercialize product candidates.

Under our collaborations with AstraZeneca, Bioverativ and Oxurion, we are responsible for identifying and optimizing *Bicycle* peptides related to collaboration targets and our collaborators are responsible for further development and product commercialization after we complete the defined research screening and compound optimization. As part of our collaboration with Cancer Research Technology Limited and CRUK, CRUK's Centre for Drug Development is sponsoring and funding a Phase I/IIa clinical trial of our lead product candidate, BT1718, in patients with advanced solid tumors. We depend on these collaborators to develop and, where applicable, commercialize products based on *Bicycle* peptides, and the success of their efforts directly impacts the milestones and royalties we will receive. We cannot assure you that our collaborators will be successful in or that they will devote sufficient resources to the development or commercialization of their products. If our current or future collaboration and commercialization partners do not perform in the manner we expect or fail to fulfill their responsibilities in a timely manner, or at all, if our agreements with them terminate or if the quality or accuracy of the clinical data they obtain is compromised, the clinical development, regulatory approval and commercialization efforts related to their and our product candidates and products could be delayed or terminated and it could become necessary for us to assume the responsibility at our own expense for the clinical development of such product candidates.

Our current collaborations and any future collaborations that we enter into are subject to numerous risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to the collaborations;
- collaborators may not perform their obligations as expected or fail to fulfill their responsibilities in a timely manner, or at all;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay preclinical studies or clinical trials, provide insufficient funding for clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our shareholders about the status of such product candidates;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- The collaborations may not result in product candidates to develop and/or preclinical studies or clinical trials conducted as part of the collaborations may not be successful;

- product candidates developed with collaborators may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to stop commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate; and

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.

In addition, certain collaboration and commercialization agreements provide our collaborators with rights to terminate such agreements, which rights may or may not be subject to conditions, and which rights, if exercised, would adversely affect our product development efforts and could make it difficult for us to attract new collaborators. In that event, we would likely be required to limit the size and scope of efforts for the development and commercialization of such product candidates or products; we would likely be required to seek additional financing to fund further development or identify alternative strategic collaborations; our potential to generate future revenue from royalties and milestone payments from such product candidates or products would be significantly reduced, delayed or eliminated; and it could have an adverse effect on our business and future growth prospects. Our rights to recover tangible and intangible assets and intellectual property rights needed to advance a product candidate or product after termination of a collaboration may be limited by contract, and we may not be able to advance a program post-termination.

If conflicts arise with our development and commercialization collaborators or licensors, they may act in their own self-interest, which may be adverse to the interests of our company.

We may in the future experience disagreements with our development and commercialization collaborators or licensors. Conflicts may arise in our collaboration and license arrangements with third parties due to one or more of the following:

- disputes with respect to milestone, royalty and other payments that are believed due under the applicable agreements;

- disagreements with respect to the ownership of intellectual property rights or scope of licenses;

- disagreements with respect to the scope of any reporting obligations;

- unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities, or to permit public disclosure of these activities; and

- disputes with respect to a collaborator's or our development or commercialization efforts with respect to our products and product candidates.

For example, we are involved in ongoing litigation with Pepscan Systems B.V., or Pepscan, related to a non-exclusive patent license agreement that we entered into with Pepscan in 2009. Pursuant to the patent license agreement, we licensed rights related to the scaffold used for *Bicycles* contained in certain of our product candidates, including our lead product candidate, BT1718. The agreement required us to enter into a framework services agreement with Pepscan for Pepscan to provide certain *Bicycles* not produced by us. In 2010, we entered into such a framework services agreement. In 2014, we terminated the framework services agreement in accordance with its terms. Subsequently, in 2016, Pepscan terminated the patent license agreement. We instituted proceedings in the District Court of The Hague to contest the right of Pepscan to terminate the patent license agreement. In response, Pepscan claimed, among other things, that the termination of the framework services agreement and alleged breach by us of confidentiality obligations constituted grounds for the termination of the patent license agreement. In a preliminary judgement delivered in April 2018, the District Court of the Hague rejected Pepscan's claim that it was entitled to terminate the patent license agreement on the basis of a breach of a purported exclusive supply obligation. The District Court of the Hague reserved for further proceedings the question of whether Pepscan was entitled to terminate the patent license agreement on the basis of allegations that we had breached our confidentiality obligations. The District Court of the Hague gave us an opportunity to submit proof to the contrary through written evidence and further hearings.

In July 2018, Pepscan appealed the decision of the District Court of the Hague and the proceedings before the District Court of the Hague have been stayed pending a decision in the appeal brought by Pepscan. While we intend to vigorously defend ourselves the appeal and any further proceedings, there can be no assurance that we will prevail. Our failure to successfully defend our use of the patent rights in question would delay the timing of our ability to commercialize our product candidates, including our lead product candidate BT1718, which could have a material adverse effect on our business and operating results.

In addition, in January 2013, Pepscan filed a notice of opposition in respect of European patent 2 257 624, which is a foundational patent that is directed to our technology platform. In April 2015, Pepscan filed a notice of opposition in respect of European patent 2 474 613, which is a divisional patent that is directed to extensions of our technology platform. As of the date of this prospectus, no final decision has been issued by the European Patent Office. If we are unable to prevail against these challenges, our intellectual property estate may be materially harmed, which would impair our ability to establish competitive barriers to entry in the form of intellectual property protections. See "Business — Legal Proceedings."

Conflicts with our development and commercialization collaborators or licensors could materially adversely affect our business, financial condition or results of operations and future growth prospects.

We rely on third parties, including independent clinical investigators and CROs, to conduct and sponsor some of the clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators, academic partners, regulatory affairs consultants and third-party CROs, to conduct our preclinical studies and clinical trials, including in some instances sponsoring such clinical trials, and to engage with regulatory authorities and monitor and manage data for our ongoing preclinical and clinical programs. For example, CRUK currently sponsors and funds the Phase I/IIa clinical trial of our lead product candidate, BT1718, in patients with advanced solid tumors. We also utilize CROs to perform toxicology studies related to our preclinical activities. While

we will have agreements governing the activities of such third parties, we will control only certain aspects of their activities and have limited influence over their actual performance. Given the breadth of clinical therapeutic areas for which we believe *Bicycles* may have utility, we intend to continue to rely on external service providers rather than build internal regulatory expertise.

Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

We remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we fail to exercise adequate oversight over any of our academic partners or CROs or if we or any of our academic partners or CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon a regulatory inspection of us, our academic partners or our CROs or other third parties performing services in connection with our clinical trials, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under applicable CGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, with respect to investigator-sponsored trials that may be conducted, we would not control the design or conduct of these trials, and it is possible that the FDA or EMA will not view these investigator-sponsored trials as providing adequate support for future clinical trials or market approval, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. We expect that such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory submissions, resulting from the investigator-sponsored trials. However, we would not

have control over the timing and reporting of the data from investigator-sponsored trials, nor would we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. Additionally, the FDA or EMA may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or EMA may require us to obtain and submit additional preclinical, manufacturing, or clinical data.

We intend to rely on third parties to manufacture product candidates, which increases the risk that we will not have sufficient quantities of such product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of the product candidates that we are developing or evaluating in our development programs. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We rely on third parties for supply of our product candidates, and our strategy is to outsource all manufacturing of our product candidates and products to third parties.

In order to conduct clinical trials of product candidates, we will need to have them manufactured in potentially large quantities. Our third-party manufacturers may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities and at any other time. For example, ongoing data on the stability of our product candidates may shorten the expiry of our product candidates and lead to clinical trial material supply shortages, and potentially clinical trial delays. If these third-party manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

Our use of new third-party manufacturers increases the risk of delays in production or insufficient supplies of our product candidates as we transfer our manufacturing technology to these manufacturers and as they gain experience manufacturing our product candidates. Even after a third-party manufacturer has gained significant experience in manufacturing our product candidates or even if we believe we have succeeded in optimizing the manufacturing process, there can be no assurance that such manufacturer will produce sufficient quantities of our product candidates in a timely manner or continuously over time, or at all.

We may be delayed if we need to change the manufacturing process used by a third party. Further, if we change an approved manufacturing process, then we may be delayed if the FDA or a comparable foreign authority needs to review the new manufacturing process before it may be used.

We operate an outsourced model for the manufacture of our product candidates, and contract with good manufacturing practice, or GMP, licensed pharmaceutical contract development and

manufacturing organizations. While we have engaged several third-party vendors to provide clinical and non-clinical supplies and fill-finish services, we do not currently have any agreements with third-party manufacturers for long-term commercial supplies. In the future, we may be unable to enter into agreements with third-party manufacturers for commercial supplies of any product candidate that we develop, or may be unable to do so on acceptable terms. Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails risks, including:

- reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control; and
- the possible termination or non-renewal of the manufacturing agreements by the third-party, at a time that is costly or inconvenient to us.

Third-party manufacturers may not be able to comply with cGMP requirements or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and/or criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. In addition, some of the product candidates we intend to develop, including BT1718, use toxins or other substances that can be produced only in specialized facilities with specific authorizations and permits, and there can be no guarantee that we or our manufacturers can maintain such authorizations and permits. These specialized requirements may also limit the number of potential manufacturers that we can engage to produce our product candidates, and impair any efforts to transition to replacement manufacturers.

Our future product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP requirements that might be capable of manufacturing for us.

If the third parties that we engage to supply any materials or manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these tests and trials while we identify and qualify replacement suppliers or manufacturers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to manufacture our product candidates, and because we collaborate with various organizations and academic institutions on the development of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets.

Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for our products and product candidates, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products and product candidates may be adversely affected.

Our ability to compete effectively will depend, in part, on our ability to maintain the proprietary nature of our technology and manufacturing processes. We rely on research, manufacturing and other know-how, patents, trade secrets, license agreements and contractual provisions to establish our intellectual property rights and protect our products and product candidates. These legal means, however, afford only limited protection and may not adequately protect our rights. As of April 2, 2019, our intellectual property portfolio includes three patent families covering novel scaffolds, 11 patent families directed to our platform technology, 63 patent families covering bicyclic peptides and related conjugates, and six patent families directed to clinical indications and other properties of development assets.

In certain situations and as considered appropriate, we have sought, and we intend to continue to seek to protect our proprietary position by filing patent applications in the United States and, in at least some cases, one or more countries outside the United States relating to current and

future products and product candidates that are important to our business. However, we cannot predict whether the patent applications currently being pursued will issue as patents, or whether the claims of any resulting patents will provide us with a competitive advantage or whether we will be able to successfully pursue patent applications in the future relating to our current or future products and product candidates. Moreover, the patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Furthermore, we, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to seek additional patent protection. It is possible that defects of form in the preparation or filing of patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If there are material defects in the form, preparation, prosecution or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents.

Even if they are unchallenged, our patents and patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected.

Other parties, many of whom have substantially greater resources and have made significant investments in competing technologies, have developed or may develop technologies that may be related or competitive with our approach, and may have filed or may file patent applications and may have been issued or may be issued patents with claims that overlap or conflict with our patent applications, either by claiming the same compositions, formulations or methods or by claiming subject matter that could dominate our patent position. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. As a result, any patents we may obtain in the future may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our products and product candidates.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that our patents are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still

may not provide protection against competing products or processes sufficient to achieve our business objectives.

In the future, one or more of our products and product candidates may be in-licensed from third parties. Accordingly, in some cases, the availability and scope of potential patent protection is limited based on prior decisions by our licensors or the inventors, such as decisions on when to file patent applications or whether to file patent applications at all. Our failure to obtain, maintain, enforce or defend such intellectual property rights, for any reason, could allow third parties, in particular, other established and better financed competitors having established development, manufacturing and distribution capabilities, to make competing products or impact our ability to develop, manufacture and market our products and product candidates, even if approved, on a commercially viable basis, if at all, which could have a material adverse effect on our business.

In addition to patent protection, we expect to rely heavily on trade secrets, know-how and other unpatented technology, which are difficult to protect. Although we seek such protection in part by entering into confidentiality agreements with our vendors, employees, consultants and others who may have access to proprietary information, we cannot be certain that these agreements will not be breached, adequate remedies for any breach would be available, or our trade secrets, know-how and other unpatented proprietary technology will not otherwise become known to or be independently developed by our competitors. If we are unsuccessful in protecting our intellectual property rights, sales of our products may suffer and our ability to generate revenue could be severely impacted.

Issued patents covering our products and product candidates could be found invalid or unenforceable if challenged in court or in administrative proceedings. We may not be able to protect our trade secrets in court.

If we initiate legal proceedings against a third-party to enforce a patent covering one of our products or product candidates, should such a patent issue, the defendant could counterclaim that the patent covering our product or product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, inter partes review and equivalent proceedings in foreign jurisdictions. An adverse determination in any of the foregoing proceedings could result in the revocation or cancellation of, or amendment to, our patents in such a way that they no longer cover our products or product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we were unaware during prosecution. If a defendant or third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our products and product candidates. Such a loss of patent protection could have a material adverse impact on our business.

For example, in January 2013, Pepscan filed a notice of opposition in respect of European patent 2 257 624, which is a foundational patent that is directed to our technology platform. In April 2015, Pepscan filed a notice of opposition in respect of European patent 2 474 613, which is a divisional patent that is directed to extensions of our technology platform. As of the date of this prospectus, no final decision has been issued by the European Patent Office. If we are unable to

prevail against these challenges, our intellectual property estate may be materially harmed, which would impair our ability to establish competitive barriers to entry in the form of intellectual property protections. See "Business — Legal Proceedings."

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach.

In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Competitors and other third parties could purchase our products and product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe, misappropriate or otherwise violate our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected or sufficient to provide an advantage over our competitors, our competitive position could be adversely affected, as could our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets.

We may be subject to claims challenging the inventorship or ownership of the patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in the patents and intellectual property that we own or that we may own or license in the future. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own or such assignments may not be self-executing or may be breached. We could be subject to ownership disputes arising, for example, from conflicting obligations of employees, consultants or others who are involved in developing our products or product candidates. Litigation may be necessary to defend against any claims challenging inventorship or ownership. If we or fail in defending any such claims, we may have to pay monetary damages and may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property, which could adversely impact our business, results of operations and financial condition.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. The terms of one or more licenses that we enter into the future may not provide us with the ability to maintain or prosecute patents in the portfolio, and must therefore rely on third parties to do so.

If we do not obtain patent term extension and data exclusivity for our products and product candidates, our business may be materially harmed.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

In the future, if we obtain an issued patent covering one of our present or future product candidates, depending upon the timing, duration and specifics of any FDA marketing approval of such product candidates, such patent may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. A patent may only be extended once and only based on a single approved product. However, we may not be granted an extension because of, for example, failure to obtain a granted patent before approval of a product candidate, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise our failure to satisfy applicable requirements. A patent licensed to us by a third party may not be available for patent term extension. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products and product candidates.

Changes in either the patent laws or the interpretation of the patent laws in the United States or other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. When implemented, the Leahy-Smith Act included several significant changes to U.S. patent law that impacted how patent rights could be prosecuted, enforced and defended. In particular, the Leahy-Smith Act also included provisions that switched the United States from a "first-to-invent" system to a "first-to-file" system, allowed third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed new regulations and procedures governing the administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. It remains unclear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent rulings from the U.S. Court of Appeals for the Federal Circuit and the U.S. Supreme Court have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We cannot assure you that our efforts to seek patent protection for one or more of our products and product candidates will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact courts' decisions in historical and future cases may have on the ability of life science companies to obtain or enforce patents relating to their products in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent rights and our ability to protect and enforce our intellectual property in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, maintaining, defending and enforcing patents on products and product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. There can be no assurance that we will obtain or maintain patent rights in or outside the United States under any future license agreements. In addition, the laws of some foreign countries do not protect

intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we pursue patent protection, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Proceedings to enforce our patent rights, even if obtained, in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. While we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds and/or methods of use for the treatment of the disease indications for which we are developing our product candidates. If any third-party patents or patent applications are found to cover our product candidates or their methods of use or manufacture, we and our collaborators or sublicensees may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all. We may also be required to indemnify our collaborators or sublicensees in such an event.

For example, we are involved in ongoing litigation with Pepscan in relation to a patent license agreement, pursuant to which we licensed rights related to the scaffold used for *Bicycles* contained in certain of our product candidates, including our lead product candidate, BT1718. While we intend to continue to vigorously defend our rights in this proceeding, there can be no assurance that we will prevail. If the outcome of these proceedings results in our inability to use the scaffold contained in certain of our product candidates, our ability to commercialize the affected product candidates, including our lead product candidate BT1718 would be impaired, which could have a material adverse effect on our business and operating results.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including interference and post-grant proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, use or manufacture of our product candidates. We cannot guarantee that any of our patent searches or analyses including, but not limited to, the identification of relevant patents, the scope of patent claims or the expiration of relevant patents are complete or thorough, nor can we be certain that we have identified each and every patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our current and former employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some

which may be competitors or potential competitors. Some of these employees may be subject to proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. For example, in the ongoing litigation with Pepscan, Pepscan claimed that we had breached certain confidentiality obligations, which was alleged to constitute sufficient grounds for the termination of our patent license agreement with Pepscan. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. In addition, our patents may become, involved in inventorship, priority, or validity disputes. To counter or defend against such claims can be expensive and time-consuming, and our adversaries may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both.

In an infringement proceeding, a court may decide that a patent is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own or control. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly. Further, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ADSs. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities.

We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we fail to comply with our obligations under any future intellectual property licenses with third parties, we could lose license rights that are important to our business.

In connection with our efforts to build our product candidate pipeline, we may enter into license agreements in the future. We expect that such license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could negatively impact the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our marks of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Employee Matters and Managing Growth

We only have a limited number of employees to manage and operate our business.

As of May 1, 2019, we had 61 full-time or part-time employees. Our focus on the development of our product candidates requires us to optimize cash utilization and to manage and operate our

business in a highly efficient manner. We cannot assure you that we will be able to hire or retain adequate staffing levels to develop our product candidates or run our operations or to accomplish all of the objectives that we otherwise would seek to accomplish.

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations.

We utilize information technology, or IT, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks, the confidentiality and the availability and integrity of our data. For example, in 2018, we were the target of a cyber-attack. The cyber-attack comprised a phishing incident where two email accounts were accessed that resulted in the automatic forwarding of emails, to an unauthorized third party. Promptly after discovery of this cyber-attack, we performed a third-party investigation and determined that no further action was required under either U.S. or state law. This incident was reported to the U.K. information commissioners' office, who deemed no further action was required under GDPR regulations. The 2018 cyber-attack did not have a material impact to our business or financial condition. While we believe we responded appropriately, including implementing remedial measures to stop this cyber-attack and with the goal of preventing similar ones in the future, there can be no assurance that we will be successful in these remedial and preventative measures or successfully mitigating the effects of future cyber-attacks. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack or destruction or loss of data could have a material adverse effect on our business and prospects. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to respond appropriately to such breaches and to implement further data protection measures.

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team and key employees, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time. We do not maintain "key person" insurance policies on the lives of these individuals or the lives of any of our other employees. The loss of the services of one or more of our current employees might impede the achievement of our research, development and commercialization objectives. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials may make it more challenging to recruit and retain qualified personnel.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

Our employees, independent contractors, consultants, collaborators and contract research organizations may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities, (2) manufacturing standards, (3) federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, and (4) laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, bribery and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee or collaborator misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. In connection with this offering, we intend to adopt a code of conduct and business ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, imprisionment, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, regulatory affairs and sales, marketing and distribution, as well as to support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified

personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to geographic areas beyond those where we have been historically located. For example, we maintain an office in Lexington, Massachusetts, at which many of our finance, management and administrative personnel work. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Risks Related to this Offering and Ownership of Our Securities

We do not know whether an active, liquid and orderly trading market will develop for our ADSs or what the market price of our ADSs will be. As a result, it may be difficult for you to sell your ADSs.

This offering constitutes the initial public offering of our ADSs, and no public market has previously existed for our ADSs or ordinary shares. We have applied to have our ADSs listed on The Nasdaq Global Market, or Nasdaq, and we expect our ADSs to be quoted on Nasdaq, subject to completion of customary procedures in the United States. Any delay in the commencement of trading of the ADSs on Nasdaq would impair the liquidity of the market for the ADSs and make it more difficult for holders to sell the ADSs.

If the ADSs are listed and quoted on Nasdaq, there can be no assurance that an active trading market for the ADSs will develop or be sustained after this offering is completed. The initial offering price will be determined by negotiations among the lead underwriters and us. Among the factors considered in determining the initial public offering price will be our future prospects and the prospects of our industry in general, our revenue, net income and certain other financial and operating information in recent periods, and the market prices of securities and certain financial and operating information of companies engaged in activities similar to ours. However, there can be no assurance that, following the completion of this offering, the ADSs will trade at a price equal to or greater than the public offering price.

The market price of our ADSs may be highly volatile, and you may not be able to resell your ADSs at or above the initial public offering price.

The market price of our ADSs following this offering is likely to be highly volatile. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your ADSs at or above the initial public offering price. The market price for our ADSs may be influenced by many factors, including:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in products similar or perceived to be similar to those we are developing or clinical trials of such products;
- an inability to obtain additional funding;
- failure by us to successfully develop and commercialize our product candidates;

- failure by us to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us to identify additional product candidates for our pipeline;
- failure by us or our licensors and strategic partners to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- an inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- the introduction of new products, services or technologies by our competitors;
- failure by us to meet or exceed financial projections we may provide to the public;
- failure by us to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic partner or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or shareholder litigation;
- changes in the market valuations of similar companies;
- sales of our ADSs or ordinary shares by us or our shareholders in the future; and
- the trading volume of our ADSs.

In addition, companies trading in the stock market in general, and Nasdaq in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ADSs, regardless of our actual operating performance.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our ADS price and trading volume could decline.

The trading market for our ADSs will likely depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. We do not currently have research coverage, and there can be no assurance that analysts will cover us, or provide favorable coverage. Securities or industry analysts may elect not to provide research coverage of our ADSs after this offering, and such lack of research coverage may negatively impact the market price of our ADSs. In the event we do have analyst coverage, if one or more analysts downgrade our ADSs or change their opinion of our ADSs, our ADS price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our ADS price or trading volume to decline.

Concentration of ownership of our ordinary shares (including ordinary shares in the form of ADSs) among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.

Our executive officers, directors, greater than five percent shareholders and their affiliates beneficially own approximately 88.7% of our ordinary shares and, upon closing of this offering, that same group will beneficially own approximately 66.0% of our outstanding ordinary shares (not accounting for any ADSs purchased in this offering by such shareholders, some of whom have indicated an interest in purchase an aggregate of approximately $25.0 million of our ADSs in this offering). Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group will be in a position to determine the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the share capital present and voting at our general meetings of shareholders may control any shareholder resolution requiring a simple majority, including the appointment of board members, certain decisions relating to our capital structure, the approval of certain significant corporate transactions and amendments to our Articles of Association. Among other consequences, this concentration of ownership may prevent or discourage unsolicited acquisition proposals that you may believe are in your best interest as one of our shareholders. Some of these persons or entities may have interests different than yours. For example, because many of these shareholders purchased their ordinary shares at prices substantially below the price at which ADSs are being sold in this offering and have held their ordinary shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other shareholders.

Future sales, or the possibility of future sales, of a substantial number of our securities could adversely affect the price of the shares and dilute shareholders.

Sales of a substantial number of our ADSs in the public market could occur at any time, subject to certain restrictions described below. If our existing shareholders sell, or indicate an intent to sell, substantial amounts of our securities in the public market, the trading price of the ADSs could decline significantly and could decline below the public offering price in this offering. Upon completion of this offering, we will have 17,696,417 outstanding ordinary shares (including ordinary shares represented by the ADSs). Substantially all of our equity securities outstanding prior to this offering are subject to a 180-day contractual lock-up or otherwise restricted from resale as a result of securities laws. The representatives of the underwriters may, in their sole discretion, permit the holders of the lock-up shares to sell shares or ADSs prior to the expiration of the lock-up agreements. See "Shares and American Depositary Shares Eligible for Future Sale." After the lock-up agreements pertaining to this offering expire, these ordinary shares will be eligible for sale in the public market, though shares are held by directors and executive officers and other affiliates and will be subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, for sales in the United States. In addition, ordinary shares subject to outstanding options under our equity incentive plans and the ordinary shares reserved for future issuance under our equity incentive plans will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations.

Moreover, after this offering, holders of an aggregate of 12,464,406 ordinary shares will have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders, as well as to cooperate in certain public offerings of such ordinary shares. In addition, we intend to register all ordinary shares that we may issue under our equity compensation plans. Once we register these ordinary shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Shares and American Depositary Shares Eligible for Future Sale" section of this prospectus.

Holders of ADSs are not treated as holders of our ordinary shares.

By participating in this offering you will become a holder of ADSs with underlying ordinary shares in a company incorporated under English law. Holders of ADSs are not treated as holders of our ordinary shares, unless they withdraw the ordinary shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of our ordinary shares, other than the rights that they have pursuant to the deposit agreement. See "Description of American Depositary Shares."

Holders of ADSs may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

ADSs are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to the right of ADS holders to cancel their ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of your ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, ADS holders may not be able to cancel their ADSs and withdraw the underlying ordinary shares when they owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities. See "Description of American Depositary Shares."

We are entitled to amend the deposit agreement and to change the rights of ADS holders under the terms of such agreement, or to terminate the deposit agreement, without the prior consent of the ADS holders.

We are entitled to amend the deposit agreement and to change the rights of the ADS holders under the terms of such agreement, without the prior consent of the ADS holders. We and the depositary may agree to amend the deposit agreement in any way we decide is necessary or advantageous to us or to the depositary. Amendments may reflect, among other things, operational changes in the ADS program, legal developments affecting ADSs or changes in the terms of our business relationship with the depositary. In the event that the terms of an amendment are materially disadvantageous to ADS holders, ADS holders will only receive 30 days' advance notice of the amendment, and no prior consent of the ADS holders is required under the deposit agreement. Furthermore, we may decide to direct the depositary to terminate the ADS facility at any time for any reason. For example, terminations may occur when we decide to list our ordinary shares on a non-U.S. securities exchange and determine not to continue to sponsor an ADS facility or when we become the subject of a takeover or a going-private transaction. If the ADS facility will terminate, ADS holders will receive at least 30 days' prior notice, but no prior consent is required from them. Under the circumstances that we decide to make an amendment to the deposit agreement that is disadvantageous to ADS holders or terminate the deposit agreement, the ADS holders may choose to sell their ADSs or surrender their ADSs and become direct holders of the underlying ordinary shares, but will have no right to any compensation whatsoever.

ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, holders and beneficial owners of ADSs irrevocably waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to the ADSs or the deposit agreement.

If this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the United States Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. It is advisable that you consult legal counsel regarding the jury waiver provision before entering into the deposit agreement.

If you or any other holders or beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, you or such other holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and/or the depositary. If a lawsuit is brought against us and/or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims, and the venue of the hearing.

No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with the U.S. federal securities laws and the rules and regulations promulgated thereunder.

You will not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise your right to vote.

Except as described in this prospectus and the deposit agreement, holders of the ADSs will not be able to exercise voting rights attaching to the ordinary shares represented by the ADSs. Under the terms of the deposit agreement, holders of the ADSs may instruct the depositary to vote the ordinary shares underlying their ADSs. Otherwise, holders of ADSs will not be able to exercise their right to vote unless they withdraw the ordinary shares underlying their ADSs to vote them in person or by proxy in accordance with applicable laws and regulations and our Articles of Association. Even so, ADS holders may not know about a meeting far enough in advance to withdraw those ordinary shares. If we ask for the instructions of holders of the ADSs, the depositary, upon timely notice from us, will notify ADS holders of the upcoming vote and arrange to deliver our voting materials to them. Upon our request, the depositary will mail to holders a shareholder meeting notice that contains, among other things, a statement as to the manner in which voting instructions may be given. We cannot guarantee that ADS holders will receive the voting materials

in time to ensure that they can instruct the depositary to vote the ordinary shares underlying their ADSs. A shareholder is only entitled to participate in, and vote at, the meeting of shareholders, provided that it holds our ordinary shares as of the record date set for such meeting and otherwise complies with our Articles of Association. In addition, the depositary's liability to ADS holders for failing to execute voting instructions or for the manner of executing voting instructions is limited by the deposit agreement. As a result, holders of ADSs may not be able to exercise their right to give voting instructions or to vote in person or by proxy and they may not have any recourse against the depositary or us if their ordinary shares are not voted as they have requested or if their shares cannot be voted.

You may not receive distributions on our ordinary shares represented by the ADSs or any value for them if it is illegal or impractical to make them available to holders of ADSs.

The depositary for the ADSs has agreed to pay to you the cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. You will receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit distribution on the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may have an adverse effect on the value of your ADSs.

Because we do not anticipate paying any cash dividends on our ADSs in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be declared and paid. Therefore, we must have distributable profits before declaring and paying a dividend. We have not paid dividends in the past on our ordinary shares. We intend to retain earnings, if any, for use in our business and do not anticipate paying any cash dividends in the foreseeable future. As a result, capital appreciation, if any, on our ADSs will be your sole source of gains for the foreseeable future, and you will suffer a loss on your investment if you are unable to sell your ADSs at or above the initial public offering price. Investors seeking cash dividends should not purchase our ADSs in this offering.

If you purchase our ADSs in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing ADSs in this offering will pay a price per ADS that substantially exceeds the net tangible book value of our ordinary shares/ADSs after the completion of this offering. As a result, investors purchasing ADSs in this offering will incur immediate dilution of $8.69 per ADS, based on the assumed initial public offering price of $15.00 per ADS, the midpoint of the price range set forth on the cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, representing the difference between the assumed initial public offering price and our pro forma as adjusted net tangible book value as of March 31, 2019 after giving effect to this offering. Further, investors purchasing ADSs in this offering will contribute approximately 33.7% of the total amount invested by shareholders since our inception, but will own only approximately 24.5% of the ordinary shares outstanding. Furthermore, if the underwriters exercise their option to purchase additional shares or our previously issued options to acquire ordinary shares at prices below the assumed initial public offering price

are exercised, you will experience further dilution. For additional information on the dilution that you will experience immediately after this offering, see the section titled "Dilution."

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our shareholders.

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under English law. Certain members of our board of directors and senior management are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States.

The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the United Kingdom. In addition, uncertainty exists as to whether U.K. courts would entertain original actions brought in the United Kingdom against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of the United Kingdom as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement.

As a result, U.S. investors may not be able to enforce against us or our senior management, board of directors or certain experts named herein who are residents of the United Kingdom or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our ADSs less attractive to investors.

We are an emerging growth company and we will remain an emerging growth company until the earlier to occur of (1) the last day of 2023, (2) the last day of the fiscal year in which we have total annual gross revenues of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a "large accelerated filer," under the rules of the U.S. Securities and Exchange

Commission, or SEC, which means the market value of our equity securities that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, or Section 404;
- not being required to comply with any requirement that has or may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- being permitted to provide only two years of audited financial statements in this initial registration statement, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and
- an exemption from the requirement to seek nonbinding advisory votes on executive compensation or golden parachute arrangements.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this prospectus. In particular, we have not included all of the executive compensation information that would be required if we were not an EGC. We cannot predict whether investors will find our ADSs less attractive if we rely on certain or all of these exemptions. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and our ADS price may be more volatile.

In addition, the JOBS Act provides that an EGC may take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" if the market value of our ordinary shares held by non-affiliates is below $250 million (or $700 million if our annual revenue is less than $100 million) as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We will incur increased costs as a result of operating as a company whose ADSs are publicly traded in the United States, and our management will be required to devote substantial time to new compliance initiatives.

As a U.S. public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance

initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk we will not be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We have identified a material weakness in our internal control over financial reporting. If we are unable to remedy the material weakness, or if we fail to establish and maintain effective internal controls, we may be unable to produce timely and accurate financial statements, and we may conclude that our internal control over financial reporting is not effective, which could adversely impact our investors' confidence and our ADS price.

We have historically been a private limited company, and as such, have not historically been subject to the reporting requirements of Section 404 or an audit performed in accordance with auditing standards issued by the PCAOB. However, in connection with the preparation of our consolidated financial statements for the year ended December 31, 2018, we identified an error in our previously reported financial statements due to a material weakness in our internal control over financial reporting related to the valuation of our warrant liability. The material weakness is attributable to a deficiency in the design and operating effectiveness of our review of the respective third party valuation reports. Specifically, the findings relate to our internal control infrastructure that existed as of December 31, 2017 and September 30, 2018 where we did not design or implement sufficient processes, controls or other review processes to ensure that the liquidation preferences of our Series A and Series B1 warrants per our articles of association were properly reflected as an input in the valuations during the year ended December 31, 2017, or for the nine month periods ended September 30, 2018 as previously reported. As a result, the financial statements for those periods required restatement.

We have implemented and are continuing to implement measures designed to improve our internal control over financial reporting to remediate the material weakness, including formalizing our processes and internal control documentation and strengthening supervisory reviews by our financial management; hiring additional qualified accounting and finance personnel and engaging financial consultants to enable the implementation of internal control over financial reporting and segregating duties amongst accounting and finance personnel. We commenced efforts to enhance our control structure by hiring a full-time corporate controller with significant U.S. GAAP, SEC reporting and biotechnology industry experience in the second quarter of 2018, as well as by engaging financial consultants to assist with the evaluation and documentation of technical

accounting matters. We expect to hire additional senior accounting staff, including those with expertise in SEC reporting and internal controls upon becoming a public company.

We expect to incur additional costs to remediate the material weakness, though there can be no assurance that our efforts will be successful or avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has ever performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our ADS price may decline as a result. We also could become subject to investigations by Nasdaq, the SEC or other regulatory authorities.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ADSs.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ADSs.

Our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an EGC, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon completion of this offering, we will become subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making

can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the TCJA, which makes significant changes to the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation and other changes that may impact our operations, in particular the operations of our wholly owned U.S. subsidiary, Bicycle Therapeutics Inc. We continue to examine the impact the TCJA may have on our business, though the effect of the TCJA on our business is uncertain. We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA on an investment in our ordinary shares or ADSs.

If we are a controlled foreign corporation, there could be adverse U.S. federal income tax consequences to certain U.S. holders.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for U.S. federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents, royalties, "global intangible low-taxed income," gains from the sale of securities and income from certain transactions with related parties. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. A non-U.S. corporation generally will be classified as a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote or 10% or more of the total value of all classes of stock of such corporation.

We believe that we were not a CFC in the 2018 taxable year and we do not expect to be a CFC in the current taxable year. However, the determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. U.S. Holders (as defined below under "Material Income Tax Considerations—Material United States Federal Income Tax Considerations for U.S. Holders") should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC.

If we are a PFIC, there could be adverse U.S. federal income tax consequences to U.S. holders.

Under the Code, we will be a PFIC, for any taxable year in which (1) 75% or more of our gross income consists of passive income or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as holding and receiving directly its proportionate share

of assets and income of such corporation. If we are a PFIC for any taxable year during which a U.S. Holder holds our shares, the U.S. Holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred and additional reporting requirements.

Based on our analysis of our income, assets, activities and market capitalization, we believe that we were a PFIC in the 2018 taxable year. We have not yet determined our PFIC status for the current taxable year, but we may be a PFIC. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies that in some circumstances are unclear and subject to varying interpretation. The value of our assets would also be determined differently for the purposes of this determination if we were treated as a CFC, as discussed above. As a result, there can be no assurance regarding if we currently are treated as a PFIC, or may be treated as a PFIC in the future. In addition, for our current and future taxable years, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our ordinary shares or ADSs from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how we spend the cash we raise in any offering, including this offering.

In certain circumstances, a U.S. Holder of shares in a PFIC may alleviate some of the adverse tax consequences described above by making either a "qualified electing fund," or QEF, election or a mark-to-market election (if our ordinary shares or ADSs constitute "marketable" securities under the Code). A U.S. Holder would be able to make a mark-to-market election with respect to our ordinary shares or ADSs as long as those shares or ADSs constitute marketable securities under the Code. However, a U.S. Holder may make a QEF election with respect to our ordinary shares or ADSs only if we agree to furnish such U.S. Holder annually with required information. If we determine that we are a PFIC for this taxable year or any future taxable year, we currently expect that we would make available the information necessary for U.S. Holders to make a QEF Election.

For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section of this prospectus entitled "Material Income Tax Considerations — Material United States Federal Income Considerations for U.S. Holders."

We may be unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments or benefit from favorable U.K. tax legislation.

As a U.K. incorporated and tax resident entity, we are subject to U.K. corporate taxation on tax-adjusted trading profits. Due to the nature of our business, we have generated losses since inception and therefore have not paid any U.K. corporation tax. As of December 31, 2018, we had cumulative carryforward tax losses of $29.1 million in the U.K. As of March 31, 2019, we had cumulative carryforward tax losses of $40.5 million in the U.K. Subject to numerous utilization criteria and restrictions (including those that limit the percentage of profits that can be reduced by carried forward losses and those that can restrict the use of carried forward losses where there is a change of ownership of more than half the ordinary shares of the company and a major change in the nature, conduct or scale of the trade), we expect these to be eligible for carry forward and utilization against future operating profits. The use of loss carryforwards in relation to U.K. profits incurred on or after April 1, 2017 will be limited each year to £5.0 million plus an incremental 50% of U.K. taxable profits. In addition, if we were to have a major change in the nature of the conduct of our trade, loss carryforwards may be restricted or extinguished.

As a company that carries out extensive research and development activities, we seek to benefit from one of two U.K. research and development tax relief programs, the Small and Medium-sized Enterprises R&D Tax Credit Program, or SME Program, and the Research and Development Expenditure program, or RDEC Program. Where available, under the SME Program, we may be able to surrender the trading losses that arise from our qualifying research and development activities for cash or carried forward for potential offset against future profits (subject to relevant restrictions). The majority of our pipeline research, clinical trials management and manufacturing development activities are eligible for inclusion within these SME Program tax credit cash rebate claims. On October 29, 2018, the U.K. government proposed that from April 1, 2020 the amount of payable credit that a qualifying loss-making SME business can receive through R&D relief in any one year will be capped at three times the company's total PAYE and NICs liability for that year.

We may benefit in the future from the United Kingdom's "patent box" regime, which allows certain profits attributable to revenues from patented products (and other qualifying income) to be taxed at an effective rate of 10%. We are the exclusive licensee or owner of several patent applications which, if issued, would cover our product candidates, and accordingly, future upfront fees, milestone fees, product revenues and royalties could be taxed at this tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. research and development tax credit regime or the "patent box" regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments then our business, results of operations and financial condition may be adversely affected.

Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.

The tax treatment of the company is subject to changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, as well as tax policy initiatives and reforms related to the Organisation for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, HM Revenue & Customs, or HMRC, the Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that

material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Shareholder protections found in provisions under the U.K. City Code on Takeovers and Mergers, or the Takeover Code, will not apply if our place of management and control is considered to change to outside the United Kingdom.

Prior to the consummation of this offering, we will re-register as a public limited company incorporated in England and Wales. Our place of central management and control is currently in the United Kingdom. Accordingly, we are currently subject to the Takeover Code and, as a result, our shareholders are entitled to the benefit of certain takeover offer protections provided under the Takeover Code. The Takeover Code provides a framework within which takeovers of companies are regulated and conducted. If, at the time of a takeover offer, the Panel on Takeovers and Mergers determines that we do not have our place of central management and control in the United Kingdom, then the Takeover Code would not apply to us and our shareholders would not be entitled to the benefit of the various protections that the Takeover Code affords. In particular, we would not be subject to the rules regarding mandatory takeover bids. The following is a brief summary of some of the most important rules of the Takeover Code:

- when any person acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares already held by that person and an interest in shares held or acquired by persons acting in concert with him or her) carry 30% or more of the voting rights of a company that is subject to the Takeover Code, that person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights in that company to acquire the balance of their interests in the company;

- when any person who, together with persons acting in concert with him or her, is interested in shares representing not less than 30% but does not hold more than 50% of the voting rights of a company that is subject to the Takeover Code, and such person, or any person acting in concert with him or her, acquires an additional interest in shares which increases the percentage of shares carrying voting rights in which he or she is interested, then such person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights of that company to acquire the balance of their interests in the company;

- a mandatory offer triggered in the circumstances described in the two paragraphs above must be in cash (or be accompanied by a cash alternative) and at not less than the highest price paid within the preceding 12 months to acquire any interest in shares in the company by the person required to make the offer or any person acting in concert with him or her;

- in relation to a voluntary offer (i.e. any offer which is not a mandatory offer), when interests in shares representing 10% or more of the shares of a class have been acquired for cash by an offeror (i.e., a bidder) and any person acting in concert with it in the offer period and the previous 12 months, the offer must be in cash or include a cash alternative for all shareholders of that class at not less than the highest price paid for any interest in shares of that class by the offeror and by any person acting in concert with it in that period. Further, if an offeror acquires for cash any interest in shares during the offer period, a cash alternative must be made available at not less than the highest price paid for any interest in the shares of that class;

- if the offeror acquires an interest in shares in an offeree company (i.e., a target) at a price higher than the value of the offer, the offer must be increased to not less than the highest price paid for the interest in shares so acquired;
- the offeree company must obtain competent advice as to whether the terms of any offer are fair and reasonable and the substance of such advice must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company;
- special or favorable deals for selected shareholders are not permitted, except in certain circumstances where independent shareholder approval is given and the arrangements are regarded as fair and reasonable in the opinion of the financial adviser to the offeree;
- all shareholders must be given the same information;
- each document published in connection with an offer by or on behalf of the offeror or offeree must state that the directors of the offeror or the offeree, as the case may be, accept responsibility for the information contained therein;
- profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisers;
- misleading, inaccurate or unsubstantiated statements made in documents or to the media must be publicly corrected immediately;
- actions during the course of an offer by the offeree company, which might frustrate the offer are generally prohibited unless shareholders approve these plans. Frustrating actions would include, for example, lengthening the notice period for directors under their service contract or agreeing to sell off material parts of the target group;
- stringent and detailed requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealing in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1% or more of any class of relevant securities; and
- employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the U.K. Companies Act, or the Companies Act, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. See "Description of Share Capital and Articles of Association — Differences in Corporate Law" in this prospectus for a description of the principal differences between the provisions of the Companies Act applicable to us and, for example, the Delaware General Corporation Law relating to stockholders' rights and protections.

The principal differences include the following:

- under English law and our articles of association, each shareholder present at a meeting has only one vote unless demand is made for a vote on a poll, in which case each holder gets one vote per share owned. Under U.S. law, each shareholder typically is entitled to one vote per share at all meetings;

- under English law, it is only on a poll that the number of shares determines the number of votes a holder may cast. You should be aware, however, that the voting rights of ADSs are also governed by the provisions of a deposit agreement with our depositary bank

- under English law, subject to certain exceptions and disapplications, each shareholder generally has preemptive rights to subscribe on a proportionate basis to any issuance of ordinary shares or rights to subscribe for, or to convert securities into, ordinary shares for cash. Under U.S. law, shareholders generally do not have preemptive rights unless specifically granted in the certificate of incorporation or otherwise;

- under English law and our articles of association, certain matters require the approval of 75% of the shareholders who vote (in person or by proxy) on the relevant resolution (or on a poll of shareholders representing 75% of the ordinary shares voting (in person or by proxy)), including amendments to the articles of association. This may make it more difficult for us to complete corporate transactions deemed advisable by our board of directors. Under U.S. law, generally only majority shareholder approval is required to amend the certificate of incorporation or to approve other significant transactions;

- in the United Kingdom, takeovers may be structured as takeover offers or as schemes of arrangement. Under English law, for so long as we continue to be subject to the Takeover Code, a bidder seeking to acquire us by means of a takeover offer would need to make an offer for all of our outstanding ordinary shares/ADSs. If acceptances are not received for 90% or more of the ordinary shares/ADSs under the offer, under English law, the bidder cannot complete a "squeeze out" to obtain 100% control of us. Accordingly, acceptances of 90% of our outstanding ordinary shares/ADSs will likely be a condition in any takeover offer to acquire us, not 50% as is more common in tender offers for corporations organized under Delaware law. By contrast, a scheme of arrangement, the successful completion of which would result in a bidder obtaining 100% control of us, requires the approval of a majority of shareholders voting at the meeting and representing 75% of the ordinary shares voting for approval;

- under English law and our articles of association, shareholders and other persons whom we know or have reasonable cause to believe are, or have been, interested in our shares may be required to disclose information regarding their interests in our shares upon our request, and the failure to provide the required information could result in the loss or restriction of rights attaching to the shares, including prohibitions on certain transfers of the shares, withholding of dividends and loss of voting rights. Comparable provisions generally do not exist under U.S. law; and

- the quorum requirement for a shareholders' meeting is a minimum of two shareholders entitled to vote at the meeting and present in person or by proxy or, in the case of a shareholder which is a corporation, represented by a duly authorized officer. Under U.S. law, a majority of the shares eligible to vote must generally be present (in person or by proxy) at a shareholders' meeting in order to constitute a quorum. The minimum number of shares required for a quorum can be reduced pursuant to a provision in a company's certificate of incorporation or bylaws, but typically not below one-third of the shares entitled to vote at the meeting.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections titled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to advance our product candidates into, and successfully complete, clinical trials;
- our reliance on the success of our product candidates in our BTC program and our other pipeline programs;
- our ability to utilize our screening platform to identify and advance additional product candidates into clinical development;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- our ability to develop sales and marketing capabilities;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate our business without infringing the intellectual property rights and proprietary technology of third parties;
- cost associated with defending intellectual property infringement, product liability and other claims;
- regulatory development in the United States, under the laws and regulations of England and Wales, and other jurisdictions;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations or obtain additional grant funding;
- the rate and degree of market acceptance of any approved products;
- developments relating to our competitors and our industry, including competing therapies;
- our ability to effectively manage our anticipated growth;

- our ability to attract and retain qualified employees and key personnel;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- statements regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance;
- our expected use of proceeds of this offering;
- the future trading price of the ADSs and impact of securities analysts' reports on these prices; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "Risk Factors" and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

MARKET, INDUSTRY AND OTHER DATA

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk Factors." These and other factors could cause our future performance to differ materially from those expressed in the industry publications, as well as from our assumptions and estimates. See the section titled "Special Note Regarding Forward-Looking Statements."

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of 4,333,333 ADSs in this offering will be approximately $57.1 million based upon an assumed initial public offering price of $15.00 per ADS, the midpoint of the price range set forth on the cover of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional ADSs in full, we estimate that our net proceeds will be approximately $66.1 million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per ADS would increase (decrease) the net proceeds to us from this offering by approximately $4.0 million, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1,000,000 ADSs offered by us would increase (decrease) the net proceeds to us from this offering by approximately $14.0 million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to create a public market for the ADSs, and to facilitate our future access to the public equity markets and obtain additional capital. We currently expect to use the net proceeds from this offering, together with our existing cash, as follows:

- approximately $35.0 million to $40.0 million to complete preparation for Phase II and III clinical development of BT1718, including manufacturing activities, and to advance BT5528 and BT8009 through Phase I and IIa clinical development;
- approximately $20.0 million to $25.0 million to advance our CD137 programs through preclinical development, including IND-enabling studies, and to advance one CD137 multimeric program through Phase I clinical development; and
- approximately $15.0 million to $20.0 million on continued drug discovery efforts and translational research;
- the remainder on further expansion of our infrastructure to support our pipeline as well as to fund working capital and other general corporate purposes.

This expected use of the net proceeds from this offering and our existing cash represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and may change the allocation of use of these proceeds among the uses described above. An investor will not have the opportunity to evaluate the economic, financial or other information on which we base our decisions on how to use the proceeds.

We may use a portion of the net proceeds of this offering for the acquisition or licensing, as the case may be, of additional technologies, other assets or businesses, or for other strategic investments or opportunities, although we have no current understandings, agreements or commitments to do so at this time. Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments, or hold as cash.

DIVIDEND POLICY

We have not declared or paid any dividends to our shareholders on our ordinary shares or our convertible preferred shares. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Investors should not purchase the ADSs with the expectation of receiving cash dividends.

Any future determination to pay dividends will be made at the discretion of our board of directors and may be based on a number of factors, including our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors that our board of directors may deem relevant. In addition, our ability to pay dividends may be limited under English law. See "Risk Factors—Because we do not anticipate paying any cash dividends on our ADSs in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment." If we pay any dividends, we will pay the ADS holders to the same extent as holders of our ordinary shares, subject to the terms of the deposit agreement, including the fees and expenses payable thereunder. See "Description of American Depositary Shares." Cash dividends on our ordinary shares, if any, will be paid in U.S. dollars.

SHARE CAPITAL REORGANIZATION AND RE-REGISTRATION

The share capital reorganization described below shall be implemented prior to the completion of this offering so that 13,363,084 ordinary shares of £0.01 nominal value each shall be in issue prior to the completion of this offering. We shall re-register Bicycle Therapeutics Limited as a public limited company and rename it Bicycle Therapeutics plc. Therefore, investors in this offering will acquire, and this prospectus only describes the offering of, ADSs each representing one ordinary share of Bicycle Therapeutics plc.

Share Capital Reorganization

To effect the share capital reorganization, Bicycle Therapeutics Limited shall capitalize a certain sum standing to the credit of Bicycle Therapeutics Limited's share premium account, and apply such sum in paying up newly issued fully paid shares by means of a bonus share issue. The calculation of the number of bonus shares to be issued will be determined based on the final price per ADS in this offering. The issue of bonus shares will vary the share capital of the Company and will also result in an adjustment to the number of: (a) warrant shares granted pursuant to the existing warrant instruments; and (b) options under the option agreements in each case to maintain the percentage interest in the Company's fully diluted share capital held by each warrant holder and option holder before the bonus shares were issued.

Reorganization of the Share Capital and Re-registration of Bicycle Therapeutics Limited as Bicycle Therapeutics plc

Prior to completion of this offering, Bicycle Therapeutics Limited will re-register as a public limited company. Such re-registration will require the passing of special resolutions by the shareholders of Bicycle Therapeutics Limited to approve the re-registration as a public company, the name change to Bicycle Therapeutics plc and the adoption of a new set of articles of association for Bicycle Therapeutics plc.

Certain further resolutions will be required to be passed by the shareholders of the Company prior to the completion of this offering, details of which are set out in the section titled "Description of Share Capital and Articles of Association."

Conditional upon and effectively immediately prior to completion of this offering, each class of shares in the issued share capital of Bicycle Therapeutics plc will be reorganized and re-designated into an aggregate of 13,363,084 shares of a single class of ordinary shares of nominal value £0.01 per ordinary share of Bicycle Therapeutics plc.

CAPITALIZATION

The following table sets forth our cash and capitalization as of March 31, 2019 on:

- an actual basis;
- a pro forma basis to give effect to (i) the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares immediately prior to the completion of this offering, (iii) the automatic conversion of all outstanding convertible preferred shares as of March 31, 2019, including those issuable upon the exercise of the warrants referenced in (i) and (ii) above, into an aggregate of 12,464,406 ordinary shares upon the completion of this offering, and (iv) the reclassification of the warrant liability into additional paid-in capital, upon the completion of this offering; and
- on a pro forma as adjusted basis giving effect to the pro forma adjustments set forth above and to give further effect to the sale of ADSs in this offering.

The pro forma as adjusted calculations assume an initial public offering price of $15.00 per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the sections titled "Selected Consolidated Financial Data," "Exchange Rate Information," "Use of

Proceeds" and "Management's Discussion and Analysis of Financial Condition and Results Of Operations."

	As of March 31, 2019		
	Actual	Pro Forma[1]	Pro Forma As Adjusted[2]
	(in thousands, except share and per share data)		
Cash	$ 59,364	$ 59,371	$ 116,451
Warrant liability	8,101	—	—
Series A convertible preferred shares, £0.01 nominal value; 3,000,001 shares authorized, 2,800,001 shares issued and outstanding at March 31, 2019, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	41,820	—	—
Series B1 convertible preferred shares, £0.01 nominal value: 4,690,485 shares authorized, 3,947,198 shares issued and outstanding at March 31, 2019, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	54,621	—	—
Series B2 convertible preferred shares, £0.01 nominal value; 1,403,633 shares authorized, issued and outstanding at March 31, 2019, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	27,339	—	—
Shareholders' (deficit) equity:			
Ordinary shares, £0.01 nominal value; 15,452,420 shares authorized, 898,678 shares issued and 842,035 shares outstanding at March 31, 2019, actual: 15,452,420 shares authorized, 13,363,084 shares issued and 13,306,441 shares outstanding at March 31, 2019, pro forma; 31,995,653 shares authorized, 17,696,417 shares issued and 17,639,774 shares outstanding, pro forma as adjusted	11	173	229
Additional paid-in capital	2,132	133,858	190,882
Accumulated other comprehensive loss	(671)	(671)	(671)
Accumulated deficit	(76,445)	(76,445)	(76,445)
Total shareholders' (deficit) equity	(74,973)	56,915	113,995
Total capitalization	$ 56,908	$ 56,915	$ 113,995

(1) The number of ordinary shares to be outstanding after this offering is based on 898,678 ordinary shares (which includes 56,643 unvested restricted shares subject to repurchase by us) outstanding as of March 31, 2019, and also gives effect to (i) the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares immediately prior to the completion of this offering, (iii) the automatic conversion of all outstanding convertible preferred shares as of March 31, 2019, including those issuable upon exercise of the warrants referenced in (i) and (ii) above, into an aggregate of 12,464,406 ordinary shares upon the completion of this offering, and (iv) the reclassification of the warrant liability into additional paid-in capital upon the completion of this offering, and excludes:

- 930,861 ordinary shares issuable upon the exercise of options to subscribe for ordinary shares outstanding as of March 31, 2019 at a weighted average exercise price of $1.33 per ordinary share;
- 627,382 ordinary shares reserved for future issuance as of March 31, 2019 in connection with equity awards, which will no longer be reserved following this offering;
- 2,470,583 ordinary shares that will be made available for future issuance under our 2019 Share Option Plan upon the effectiveness of the registration statement of which this prospectus forms a part (from which we intend to grant options to purchase an aggregate of 1,311,061 ordinary shares to certain of our directors and officers upon the effectiveness of the registration of which this prospectus forms a part); and
- 215,000 ordinary shares that will be made available for future issuance under our 2019 Employee Share Purchase Plan, upon the effectiveness of the registration statement of which this prospectus forms a part.

(2) The pro forma as adjusted information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, total shareholders' (deficit) equity and total capitalization by $4.0 million, assuming that the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same. Each increase (decrease) of 1,000,000 in the number of ADSs offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, total shareholders' (deficit) equity and total capitalization by $14.0 million, assuming no change in the initial public offering price per ADS.

DILUTION

If you invest in the ADSs in this offering, your interest will be diluted to the extent of the difference between the initial public offering price per ADS and the pro forma as adjusted net tangible book value per ordinary share/ADS immediately after this offering. Dilution results from the fact that the initial public offering price per ADS is substantially in excess of the net tangible book value per ordinary share/ADS.

Our net tangible book value as of March 31, 2019 was $(77.3) million, or $(86.00) per ordinary share/ADS. Net tangible book value represents our total assets less our total liabilities and the carrying value of our convertible preferred shares, excluding deferred offering costs, and net tangible book value per share as of March 31, 2019 represents net tangible book value divided by the 898,678 ordinary shares outstanding, including 56,643 unvested restricted shares subject to repurchase by us.

Our pro forma net tangible book value as of March 31, 2019 was $54.6 million, or $4.09 per share/ADS. Pro forma net tangible book value per share is calculated after giving effect to (i) the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares immediately prior to the completion of this offering, (iii) the automatic conversion of all outstanding preferred shares as of March 31, 2019, including those issuable upon the exercise of the warrants referenced in (i) and (ii) above, into an aggregate of 12,464,406 ordinary shares upon the completion of this offering, and (iv) the reclassification of the warrant liability into additional paid-in capital upon the completion of this offering.

After giving further effect to our issuance and sale of 4,333,333 ADSs in this offering at the assumed initial public offering price of $15.00 per ADS, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2019 would have been $111.7 million, or $6.31 per share/ADS.

This represents an immediate increase in pro forma as adjusted net tangible book value per ordinary share of $2.23 to existing shareholders and immediate dilution in pro forma as adjusted net tangible book value per ADS of $8.69 to new investors purchasing ADSs in this offering. Dilution per ADS to new investors is determined by subtracting pro forma as adjusted net tangible book value per ADS after this offering from the initial public offering price per ADS paid by new investors. The following table illustrates this dilution:

Assumed initial public offering price		$ 15.00
Historical net tangible book value per ADS as of March 31, 2019	$ (86.00)	
Pro forma increase in net tangible book value per ADS as of March 31, 2019	90.09	
Pro forma net tangible book value per ADS as of March 31, 2019	4.09	
Increase in pro forma net tangible book value per ADS attributable to new investors	2.23	
Pro forma as adjusted net tangible book value per ADS after this offering		6.31
Dilution per ADS to investors participating in this offering		$ 8.69

Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per ADS, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the dilution to new investors by $0.77 per ADS, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated expenses payable by

us. An increase of 1,000,000 ADSs offered by us would decrease the dilution to new investors by $0.41 per ADS, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated expenses payable by us. A decrease of 1,000,000 ADSs offered by us would increase the dilution to new investors by $0.46 per ADS, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated expenses payable by us.

If the underwriters exercise their option to purchase additional ADSs in full, the pro forma as adjusted net tangible book value would be $6.58 per ordinary share/ADS, and the dilution in pro forma as adjusted net tangible book value to investors in this offering would be $8.42 per ADS.

The following table summarizes, on a pro forma as adjusted basis as of March 31, 2019, the differences between existing shareholders, including holders of our convertible preferred shares, and new investors with respect to the number of ordinary shares (in the form of ADSs or shares) purchased from us, the total consideration paid and the average price per ordinary share/ADS paid before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, at an assumed initial public offering price of $15.00 per ADS, which is the midpoint of the price range set forth on the cover of this prospectus.

The total number of ordinary shares does not include ordinary shares underlying the ADSs issuable upon the exercise of the option to purchase additional ADSs granted to the underwriters.

	Ordinary Shares (ADSs) Purchased		Total Consideration		Average Price per Ordinary Share/ADS
	Number	Percent	Amount	Percent	
Existing shareholders	13,363,084	75.5%	$ 128,025,000	66.3%	$ 9.58
New investors	4,333,333	24.5%	65,000,000	33.7%	$ 15.00
Total	17,696,417	100%	$ 193,025,000	100%	

Certain of our existing shareholders and their affiliated entities, including those affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $25.0 million of ADSs in this offering at the initial public offering price per ADS and on the same terms as the other purchasers in this offering. The table above does reflect any potential purchases by such shareholders in this offering.

The tables and calculations above are based on 898,678 ordinary shares (which includes 56,643 unvested restricted shares subject to repurchase by us) outstanding as of March 31, 2019, and also gives effect to (i) the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares immediately prior to the completion of this offering, and (iii) the automatic conversion of all outstanding convertible preferred shares as of March 31, 2019, including those issuable upon the exercise of the warrants referenced in (i) and (ii) above, into an aggregate of 12,464,406 ordinary shares upon completion of this offering, and excludes:

- 930,861 ordinary shares issuable upon the exercise of options to subscribe for ordinary shares outstanding as of March 31, 2019 at a weighted average exercise price of $1.33 per ordinary share;
- 627,382 ordinary shares reserved for future issuance as of March 31, 2019 in connection with equity awards, which shares will no longer be reserved following this offering;

- 2,470,583 ordinary shares that will be made available for future issuance under our 2019 Share Option Plan upon the effectiveness of the registration statement of which this prospectus forms a part (from which we intend to grant options to purchase an aggregate of 1,311,061 ordinary shares to certain of our directors and officers upon the effectiveness of the registration of which this prospectus forms a part); and

- 215,000 ordinary shares that will be made available for future issuance under our 2019 Employee Share Purchase Plan, upon the effectiveness of the registration statement of which this prospectus forms a part.

The pro forma information discussed above is illustrative only. Our net tangible book value following the closing of this offering is subject to adjustment based on the actual initial public offering price of the ADSs and other terms of this offering determined at pricing.

To the extent that outstanding options and warrants are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our shareholders.

SELECTED CONSOLIDATED FINANCIAL DATA

The following tables present the selected consolidated financial data as of the dates and for the periods indicated for Bicycle Therapeutics Limited. We derived the selected consolidated statements of operations and comprehensive loss data for the years ended December 31, 2017 and 2018 and the consolidated balance sheet data as of December 31, 2017 and 2018 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical audited consolidated financial statements as of and for the year ended December 31, 2017 have been restated. See Note 1 to the audited consolidated financial statements included elsewhere in this prospectus. The consolidated statements of operations data for the three months ended March 31, 2018 and 2019 and the consolidated balance sheet data as of March 31, 2019 have been derived from our unaudited consolidated financial statements included elsewhere in this prospectus and have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of the financial information contained in those statements. We prepare our consolidated financial statements in accordance with U.S. GAAP.

Our historical results are not necessarily indicative of our future results and our operating results for the interim period ended March 31, 2019 are not necessarily indicative of the results that may be expected for the full year ending December 31, 2019 or any other interim period or any future period. You should read this data together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information under the sections titled "Capitalization" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

The functional currency of Bicycle Therapeutics Limited and its wholly owned subsidiaries in the United Kingdom, BicycleTx Limited and BicycleRD Limited, is the pound sterling. The functional currency of Bicycle Therapeutics Inc. is the U.S. dollar. For financial reporting purposes, the financial statements of Bicycle Therapeutics Limited, BicycleTx Limited and BicycleRD Limited, which are prepared using the functional currency, have been translated into U.S. dollars. Our assets and liabilities are translated at the exchange rates at the balance sheet date, our revenue and expenses are translated at average exchange rates and shareholders' (deficit) equity is translated based on historical exchange rates. Translation adjustments are not included in determining net loss but are included in foreign exchange translation adjustment within accumulated other comprehensive income (loss), a component of shareholders' (deficit) equity.

Foreign currency transactions in currencies different from the functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss.

As of March 29, 2019, the last business day of the three months ended March 31, 2019, the representative exchange rate was $1.3032 = £1.00.

Prior to the completion of this offering, we intend to reorganize our share capital and re-register Bicycle Therapeutics Limited as a public limited company and to change our name from Bicycle Therapeutics Limited to Bicycle Therapeutics plc. See "Share Capital Reorganization and Re-Registration."

	Year ended December 31,		Three months ended March 31,	
	2017	2018	2018	2019
	(as restated)			
	(in thousands, except share and per share data)			
Statement of Operations Data:				
Collaboration revenues	$ 2,060	$ 7,136	$ 2,808	$ 6,384
Operating expenses:				
Research and development	11,866	20,761	3,709	6,276
General and administrative	6,407	8,121	1,988	3,402
Total operating expenses	18,273	28,882	5,697	9,678
Loss from operations	(16,213)	(21,746)	(2,889)	(3,294)
Other income (expenses):				
Interest and other income (expense)	50	169	(3)	64
Other expense, net	(119)	(665)	(38)	(3,193)
Total other expense, net	(69)	(496)	(41)	(3,129)
Net loss before income tax provision	(16,282)	(22,242)	(2,930)	(6,423)
Provision for (benefit from) income taxes	(23)	(396)	(396)	80
Net loss	$ (16,259)	$ (21,846)	$ (2,534)	$ (6,503)
Net loss attributable to ordinary shareholders	$ (16,259)	$ (21,846)	$ (2,534)	$ (6,503)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (48.81)	$ (49.78)	$ (6.38)	$ (7.80)
Weighted average ordinary shares outstanding, basic and diluted	333,125	438,862	397,483	834,043
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted (unaudited)		$ (1.93)		$ (0.25)
Pro forma weighted average number of ordinary shares outstanding, basic and diluted (unaudited)		10,954,310		13,293,400

See Note 2 within the notes to our consolidated financial statements appearing at the end of this prospectus for a description of the method used to calculate basic and diluted net loss per share applicable to ordinary shareholders and unaudited pro forma basic and diluted net loss per share.

	As of December 31,		As of March 31,
	2017	2018	2019
	(as restated)		
	(in thousands)		
Balance Sheet Data:			
Cash	$ 67,663	$ 63,380	$ 59,364
Working capital	62,061	67,840	61,500
Total assets	74,001	81,626	77,794
Total deferred revenue	14,467	14,635	9,604
Warrant liability	4,411	4,804	8,101
Convertible preferred shares	96,441	122,197	123,780
Total shareholders' deficit	$ (47,184)	$ (69,826)	$ (74,973)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read this discussion and analysis of our financial condition and consolidated results of operations together with the consolidated financial statements, related notes and other financial information included in this prospectus. Our historical consolidated financial statements as of and for the year ended December 31, 2017 have been restated. See Note 1 to the consolidated financial statements included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including statements of our plans, objectives, expectations and intentions, contain forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biopharmaceutical company developing a novel class of medicines, which we refer to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint is designed to confer high affinity and selectivity and the relatively large surface area presented by the molecule allows targets to be drugged that have historically been intractable to non-biological approaches. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic, or PK, properties of a small molecule. *Bicycles* are excreted by the kidney rather than the liver and have shown no signs of immunogenicity to date, which we believe together support a favorable toxicological profile.

We have a novel and proprietary phage display screening platform which we use to identify *Bicycles* in an efficient manner. The platform initially displays linear peptides on the surface of engineered bacteriophages, or phages, before "on-phage" cyclization with a range of small molecule scaffolds which can confer differentiated physicochemical and structural properties. Our platform encodes quadrillions of potential *Bicycles* which can be screened to identify molecules for optimization to potential product candidates. We have used this powerful screening technology to identify our current portfolio of candidates in oncology and intend to use it in conjunction with our collaborators to seek to develop additional future candidates across a range of other disease areas.

Our initial internal programs are focused on oncology indications with high unmet medical need. Our lead product candidate, BT1718, is a *Bicycle* Toxin Conjugate, or BTC. This *Bicycle* is being developed to target tumors that express Membrane Type 1 matrix metalloprotease, or MT1-MMP. MT1-MMP is expressed in approximately 76% to 96% of the ovarian, bladder, endometrial and triple negative breast cancer samples we have tested, depending on cancer type. The *Bicycle* is chemically attached to a toxin that when administered is cleaved from the *Bicycle* and kills the tumor cells. BT1718 is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial in collaboration with, and fully funded by, the Centre for Drug Development of Cancer Research UK, or CRUK. We expect to report preliminary data from the Phase I part of this clinical trial in the second half of 2019. We are also developing BT5528 and BT8009, which are BTCs targeting Ephrin type-A receptor 2, or EphA2, and Nectin-4, respectively, for oncology indications. BT5528 and BT8009 are being investigated for safety, activity and to establish a rationale for therapeutic use in preclinical studies. We are currently conducting Investigational New Drug application, or IND, -enabling activities for BT5528 and BT8009. Our discovery pipeline in oncology includes *Bicycle*-targeted innate immune activators as well as T-cell modulators.

Beyond oncology, we are collaborating with biopharmaceutical companies and organizations in therapeutic areas where we believe our proprietary *Bicycle* screening platform can identify therapies to treat diseases with significant unmet medical need. Our partnered programs outside of oncology include collaborations for anti-bacterial, cardiovascular, hematology, ophthalmology and respiratory indications.

Financial Overview

Since our inception, we have devoted substantially all of our resources to developing our *Bicycle* platform and our lead product candidates, BT1718, BT5528 and BT8009, conducting research and development of our product candidates and preclinical programs, raising capital and providing general and administrative support for our operations. To date, we have financed our operations primarily with proceeds from the sale of convertible preferred shares, as well as proceeds received from upfront payments, research and development payments, and development milestone payments from our collaboration agreements with Oxurion, AstraZeneca and Bioverativ (a Sanofi Company). Since our inception in 2009 through March 31, 2019, we have received gross proceeds of $128.0 million from the sale of convertible preferred shares, and $26.5 million of cash payments under our collaboration revenue arrangements including $4.1 million from Oxurion, $7.7 million from AstraZeneca and $14.7 million from Bioverativ. We do not have any products approved for sale and have not generated any revenue from product sales.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were $16.3 million and $21.8 million for the years ended December 31, 2017 and December 31, 2018, respectively and $6.5 million for the three months ended March 31, 2019. As of December 31, 2018 and March 31, 2019, we had an accumulated deficit of $69.9 million and $76.4 million, respectively. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future.

We anticipate that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates and, if any product candidates are approved, pursue the commercialization of such product candidates by building internal sales and marketing capabilities. In addition, we expect to incur additional costs associated with operating as a public company following the completion of this offering, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company. We expect that our expenses and capital requirements will increase substantially if and as we:

- continue our development of our product candidates, including conducting future clinical trials of BT1718;
- progress the preclinical and clinical development of BT5528 and BT8009;
- seek to identify and develop additional product candidates;
- develop the necessary processes, controls and manufacturing data to obtain marketing approval for our product candidates and to support manufacturing to commercial scale;
- develop, maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;

- hire and retain additional personnel, such as non-clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, commercial and scientific personnel;
- acquire or in-license other products and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base, including adding equipment and infrastructure to support our research and development; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs, any future commercialization efforts and our transition to operating as a public company following the completion of this offering.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain marketing approval for one or more of our product candidates, which we expect will take many years and is subject to significant uncertainty. We have no commercial-scale manufacturing facilities of our own, and all of our manufacturing activities have been and are planned to be contracted out to third parties. Additionally, we currently utilize third-party contract research organizations, or CROs, to carry out our clinical development activities. If we seek to obtain marketing approval for any of our product candidates from which we obtain promising results in clinical development, we expect to incur significant commercialization expenses as we prepare for product sales, marketing, manufacturing, and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances, charitable grants, monetization transactions or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of March 31, 2019, we had cash of $59.4 million. We believe that the anticipated net proceeds from this offering, together with our existing cash, will enable us to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our available capital resources sooner than we expect. See "— Liquidity and Capital Resources." To finance our operations beyond that point, we will need to raise additional capital, which cannot be assured.

Components of Our Results of Operations

Collaboration Revenues

To date, we have not generated any revenue from product sales and we do not expect to generate any revenue from product sales for the foreseeable future. Our revenue consists of

collaboration revenue under our arrangements with AstraZeneca, Bioverativ and Oxurion, including amounts that are recognized related to upfront payments, milestone payments, option exercise payments, and amounts due to us for research and development services. In the future, revenue may include additional milestone payments, option exercise payments, and royalties on any net product sales under our collaborations. We expect that any revenue we generate will fluctuate from period to period as a result of the timing and amount of license, research and development services, and milestone and other payments.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research and development activities, including our discovery efforts, and the development of our product candidates, which include:

- employee-related expenses including salaries, benefits, and share-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, preclinical activities, clinical activities and manufacturing on our behalf;
- the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical study materials and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs.

Research and development costs are expensed as incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as a prepaid expense or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

U.K. research and development tax credits and government grant funding are recorded as an offset to research and development expense. See "—Benefit from Income Taxes."

Our direct external research and development expenses are tracked on a program-by-program basis and consist of costs, such as fees paid to consultants, contractors and contract manufacturing organizations, or CMOs, in connection with our preclinical and clinical development activities. Costs incurred after a product candidate has been designated and that are directly related to the product candidate are included in direct research and development expenses for that program. Costs incurred prior to designating a product candidate are included in other discovery and platform related expense. We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified.

In December, 2016, we entered into a Clinical Trial and License Agreement with the Cancer Research Technology Limited, or CRTL and Cancer Research UK, or CRUK, whereby the CRUK's

Centre for Drug Development is sponsoring and funding a Phase I/IIa clinical trial for our lead product candidate, BT1718, in patients with advanced solid tumors. CRUK has designed and prepared and is carrying out and sponsoring the clinical trial at its own cost. Upon the completion of the Phase I/IIa clinical trial, we have the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and we decide to abandon development of all products that deliver cytotoxic payloads to the MT1 target antigen, we will assign or grant to Cancer Research Technology Limited an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case we will receive tiered royalties of 70% to 90% of the net revenue depending on the stage of development when the license is granted is less certain costs, as defined by the agreement). The CRUK agreement contains additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash and shares, with an aggregate total value of $50.9 million, as well as royalty payments based on a single digit percentage on net sales of products developed. Upon the completion of the Phase IIa part of the clinical trial, we expect research and development expenses to increase significantly as we expect to fund the continued development of BT1718, as well as incur additional development milestone payments.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future as a result of our expanded portfolio of product candidates and as we: (i) continue the clinical development and obtain marketing approval for our product candidates, including BT1718; (ii) initiate clinical trials for our product candidates, including BT5528 and BT8009; and (iii) build our in-house process development and analytical capabilities and continue to discover and develop additional product candidates.

The successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates. This is due to the numerous risks and uncertainties associated with developing products, including the uncertainty of:

- completing research and preclinical development of our product candidates, including conducting future clinical trials of BT1718;
- progressing the preclinical and clinical development of BT5528 and BT8009;
- establishing an appropriate safety profile with IND-enabling studies to advance our preclinical programs into clinical development;
- identifying new product candidates to add to our development pipeline;
- successful enrollment in, and the initiation and completion of clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with others;
- establishing commercial manufacturing capabilities or making arrangements with third party manufacturers;

- the development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials;
- addressing any competing technological and market developments, as well as any changes in governmental regulations;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations under such arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how, as well as obtaining and maintaining regulatory exclusivity for our product candidates;
- continued acceptable safety profile of the drugs following approval; and
- attracting, hiring and retaining qualified personnel.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, the FDA, EMA or another regulatory authority may require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or we may experience significant trial delays due to patient enrollment or other reasons, in which case we would be required to expend significant additional financial resources and time on the completion of clinical development. In addition, we may obtain unexpected results from our clinical trials and we may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, travel expenses and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

Foreign currency transactions in currencies different from the functional currency of our UK entities are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates in foreign currencies are recorded in general and administrative expense in the statement of operations and comprehensive loss. As such, our operating expenses may be impacted by future changes in exchange rates. See "*Quantitative and Qualitative Disclosures About Market Risks*" for further discussion.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development and potential commercialization of our portfolio of product candidates. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, information systems, legal, regulatory and tax compliance services, director and officer insurance costs and investor and public relations costs.

Other Income (Expense)

Interest and Other Income

Interest and other income consists primarily of interest earned on our cash held in operating accounts.

Other Expense

Other expense, consists primarily of changes in the fair value associated with the remeasurement of the warrant liability for warrants we issued to subscribe for Series A and Series B1 convertible preferred shares. We will continue to remeasure the warrant liability at fair value at each reporting period. We expect the warrant liability to increase until the completion of this offering. Upon the completion of this offering, the respective warrants will expire or will be exercised, and as such, we do not expect to incur additional expense related to the remeasurement of the warrant liability subsequent to this offering.

Provision For (Benefit From) Income Taxes

We are subject to corporate taxation in the United States and the United Kingdom. We have generated losses since inception and have therefore not paid United Kingdom corporation tax. The income tax provision for (benefit from) presented in our consolidated statements of operations and comprehensive loss represents the tax impact from our operating activities in the United States, which has generated taxable income in certain periods based on intercompany service arrangements.

The research and development tax credit received in the U.K. is recorded as a reduction to research and development expenses. The U.K. research and development tax credit, as described below, is fully refundable to us after surrendering tax losses and is not dependent on current or future taxable income. As a result, we have recorded the entire benefit from the U.K. research and development tax credit as a reduction to research and development expenses and is not reflected as part of the income tax provision. If, in the future, any U.K. research and development tax credits generated are needed to offset a corporate income tax liability in the U.K., that portion would be recorded as a benefit within the income tax provision and any refundable portion not dependent on taxable income would continue to be recorded as a reduction to research and development expenses.

As a company that carries out extensive research and development activities, we seek to benefit from one of two U.K. research and development tax credit cash rebate regimes: The Small and Medium-sized Enterprises R&D Tax Credit Program, or SME Program, and the Research and Development Expenditure program, or RDEC Program. Qualifying expenditures largely comprise employment costs for research staff, consumables expenses incurred under agreements with third parties that conduct research and development, preclinical activities, clinical activities and manufacturing on our behalf and certain internal overhead costs incurred as part of research projects.

Based on criteria established by U.K. law, a portion of expenditures being carried out in relation to our pipeline research and development, clinical trials management and manufacturing development activities are to be eligible for the RDEC Program for the year ended December 31, 2018. We will assess whether it is possible to qualify under the more favorable SME regime for future accounting periods, but this will be affected as a result of becoming a large company by reference to our staff headcount and/or our financial results.

Unsurrendered U.K. losses may be carried forward indefinitely to be offset against future taxable profits, subject to numerous utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of U.K. taxable profits. After accounting for tax credits receivable, we had accumulated tax losses for carry forward in the U.K. of $29.1 million as of December 31, 2018 and $40.5 million as of March 31, 2019.

Value Added Tax, or VAT, is broadly charged on all taxable supplies of goods and services by VAT-registered businesses. Under current rates, an amount of 20% of the value, as determined for VAT purposes, of the goods or services supplied is added to all sales invoices and is payable to HMRC. Similarly, VAT paid on purchase invoices is generally reclaimable from HMRC and is included as a component of prepaid and other current assets in our consolidated balance sheet.

Results of Operations

Comparison of the Years Ended December 31, 2017 and 2018

The following table summarizes our results of operations for the years ended December 31, 2017 and 2018:

	Year Ended December 31,		
	2017 (as restated)	2018	Change
	(in thousands)		
Collaboration revenues	$ 2,060	$ 7,136	$ 5,076
Operating expenses:			
Research and development	11,866	20,761	8,895
General and administrative	6,407	8,121	1,714
Total operating expenses	18,273	28,882	10,609
Loss from operations	(16,213)	(21,746)	(5,533)
Other income (expenses):			
Interest and other income	50	169	119
Other expense	(119)	(665)	(546)
Total other expense, net	(69)	(496)	(427)
Net loss before income tax provision	(16,282)	(22,242)	(5,960)
Benefit from income taxes	(23)	(396)	(373)
Net loss	$ (16,259)	$ (21,846)	$ (5,587)

Collaboration Revenues

Collaboration revenues increased by $5.1 million during the year ended December 31, 2018 compared to the year ended December 31, 2017, primarily due to increases of $3.7 million of revenue from our collaboration with Bioverativ and $0.5 million of revenue under the AstraZeneca collaboration agreement as the year ended December 31, 2017 included less than a year of collaboration activities for both arrangements. In addition, revenue under our collaboration agreement with Oxurion increased by $0.9 million due to $0.5 million of additional research services performed in the year ended December 31, 2018 pursuant to an amendment to the collaboration agreement, as well as incremental revenue related to the achievement of developmental milestones of $0.4 million for the advancement of the research by Oxurion into a Phase I clinical trial.

Research and Development Expenses

The table below summarizes our research and development expenses for the period:

	Year Ended December 31,		
	2017 (as restated)	2018	Change
	(in thousands)		
BT1718 (MT1)	$ 2,361	$ 1,546	$ (815)
BT5528 (EphA2)	—	4,569	4,569
BT8009 (Nectin-4)	—	2,797	2,797
Other discovery and platform related expense	7,796	8,702	906
Employee and contractor related expenses	3,784	7,698	3,914
Facility expenses	798	1,328	530
Research and development incentives	(2,873)	(5,879)	(3,006)
Total research and development expenses	$ 11,866	$ 20,761	$ 8,895

Research and development expense increased by $8.9 million in the year ended December 31, 2018 as compared to the prior year, primarily due to increases of $4.6 million and $2.8 million in the BT5528 and BT8009 program spending, respectively, as we nominated candidates for these development programs in 2018, as well as an increase of $0.9 million in other unallocated discovery and platform related expense, an increase of $3.9 million in employee and contractor related expenses, and an increase of $0.5 million in facilities related expenses due to an increase in headcount as we expanded our operations in the United States and the United Kingdom. These expenses were offset by a decrease in program spending on BT1718 of $0.8 million due to the timing of clinical material manufacturing, as well as an increase in the research and development tax credit reimbursement of $3.0 million, due to the corresponding increase in research and development spending in the United Kingdom.

We begin to separately track program expenses at candidate nomination, at which point we will accumulate all costs to support that program to date. Through December 31, 2018, since the candidate nominations of BT1718, BT5528 and BT8009, we have incurred approximately $11.7 million, $4.6 million and $2.8 million of direct expenses for the development of these programs, respectively.

General and Administrative Expenses

General and administrative expenses were $8.1 million for the year ended December 31, 2018, compared to $6.4 million for the year ended December 31, 2017. The increase of $1.7 million primarily reflected increases of $1.5 million in personnel related costs, $0.2 million in facilities related costs, and $1.0 million in professional fees. These increases were due to the hiring of additional personnel in our general and administrative functions as we expanded our operations in the United States and the United Kingdom. These amounts were offset by an increase in gains from the effect of foreign exchange rates of $0.9 million during year ended December 31, 2018.

Other Expense, net

Other expense, net increased by $0.4 million during the year ended December 31, 2018, compared to year ended December 31, 2017, primarily due to additional expense of $0.7 million related to the re-measurement associated with changes in the fair value of the warrant liability for warrants to subscribe for Series A and Series B1 convertible preferred shares. This was offset by an

increase in interest income as a result of higher cash balances in 2018 following the closing of our Series B1 financings in May and October of 2017 and Series B2 financing in December 2018.

Comparison of the Three Months Ended March 31, 2018 and 2019

The following table summarizes our results of operations for the three months ended March 31, 2018 and 2019:

	Three months Ended March 31,		
	2018	2019	Change
	(in thousands)		
Collaboration revenues	$ 2,808	$ 6,384	$ 3,576
Operating expenses:			
Research and development	3,709	6,276	2,567
General and administrative	1,988	3,402	1,414
Total operating expenses	5,697	9,678	3,981
Loss from operations	(2,889)	(3,294)	(405)
Other income (expenses):			
Interest and other income (expense)	(3)	64	67
Other expense, net	(38)	(3,193)	(3,155)
Total other expense, net	(41)	(3,129)	(3,088)
Net loss before income tax provision	(2,930)	(6,423)	(3,493)
Provision for (benefit from) income taxes	(396)	80	476
Net loss	$ (2,534)	$ (6,503)	$ (3,969)

Collaboration Revenues

Collaboration revenues increased by $3.6 million in the three months ended March 31, 2019 compared to the three months ended March 31, 2018, primarily due to an increase of $4.8 million of revenue from our collaboration with Bioverativ. In March 2019, Bioverativ exercised its right to terminate the sickle cell program, as such, amounts that were previously deferred and allocated to a material right of $5.3 million were recognized into revenue during the three months ended March 31, 2019. This was offset by a decrease of $1.4 million of revenue under our collaboration agreement with Oxurion primarily due to revenue recognized of $1.2 million for certain development milestones achieved during the three months ended March 31, 2018 that did not recur in the three months ended March 31, 2019.

Research and Development Expenses

The table below summarizes our research and development expenses for the period:

	Three Months Ended March 31,		
	2018	2019	Change
	(in thousands)		
BT1718 (MT1)	$ 175	$ 448	$ 273
BT5528 (EphA2)	356	783	427
BT8009 (Nectin-4)	281	1,086	805
Other discovery and platform related expense	1,702	3,064	1,362
Employee and contractor related expenses	1,655	2,245	590
Facility expenses	375	300	(75)
Research and development incentives	(835)	(1,650)	(815)
Total research and development expenses	$ 3,709	$ 6,276	$ 2,567

Research and development expense increased by $2.6 million in the three months ended March 31, 2019 compared to the three months ended March 31, 2018, primarily due to increases of $0.8 million and $0.4 million in the BT8009 and BT5528 program spending, respectively, due to increased spending for these development programs in 2019 related to IND-enabling preclinical studies. In addition, the overall increase in research and development expense includes a $0.3 million increase in BT1718 development expenses, an increase of $1.4 million in other unallocated discovery and platform related expense, and an increase of $0.6 million in employee and contractor related expenses due to an increase in headcount as we expanded our operations in the United States and the United Kingdom. These expenses were offset by a decrease in facilities-related expenses of $0.1 million, as well as an increase in the research and development tax credit reimbursement of $0.8 million, due to the corresponding increase in research and development spending in the United Kingdom.

We begin to separately track program expenses at candidate nomination, at which point we will accumulate all costs to support that program to date. Through March 31, 2019, since the candidate nominations of BT1718, BT5528 and BT8009, we have incurred approximately $12.1 million, $5.4 million and $3.9 million of expenses for the development of these programs, respectively.

General and Administrative Expenses

General and administrative expenses were $3.4 million for the three months ended March 31, 2019, compared to $2.0 million for the three months ended March 31, 2018. The increase of $1.4 million primarily reflected increases of $0.5 million in personnel related costs due to the hiring of additional personnel as we expanded our operations in the United States and the United Kingdom, as well as an increase of $0.8 million in professional fees, including legal, human resources, marketing and consulting costs as we prepared to become a public company.

Other Expense, net

Other expense, net increased by $3.1 million during the three months ended March 31, 2019, compared to the three months ended March 31, 2018, due primarily to the re-measurement associated with changes in the fair value of the warrant liability associated with our outstanding warrants to subscribe for Series A and Series B1 convertible preferred shares. This was partially offset by a small increase in interest income as a result of higher cash balances on hand following

the closing of our Series B2 financing and receipts of cash from our collaboration arrangements with AstraZeneca and Bioverativ.

Liquidity and Capital Resources

From our inception through March 31, 2019, we have not generated any revenue from product sales and incurred significant operating losses and negative cash flows from our operations. We do not expect to generate significant revenue from sales of any products for several years, if at all.

To date, we have financed our operations primarily with proceeds from the sale of convertible preferred shares, as well as proceeds received from upfront payments, payments for research and development services, and development milestone payments from our collaboration agreements with AstraZeneca, Oxurion and Bioverativ.

Since our inception in 2009 through March 31, 2019, we have received gross proceeds of $128.0 million from the sale of convertible preferred shares, and $26.5 million of payments under our collaboration revenue arrangements including $4.1 million from Oxurion, $7.7 million from AstraZeneca and $14.7 million from Bioverativ.

Cash Flows

The following table summarizes our cash flows for each of the periods presented:

	Year Ended December 31,		Three Months Ended March 31,	
	2017	2018	2018	2019
	(as restated)			
	(in thousands)			
Net cash used in operating activities	$ (1,415)	$ (26,078)	$ (7,273)	$ (5,201)
Net cash used in investing activities	(1,113)	(1,186)	(264)	(418)
Net cash provided by financing activities	57,876	25,430	—	34
Effect of exchange rate changes on cash	2,913	(2,449)	2,432	1,569
Net increase (decrease) in cash	$ 58,261	$ (4,283)	$ (5,105)	$ (4,016)

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2018 included our net loss of $2.5 million, net cash used by changes in our operating assets and liabilities of $5.2 million and non-cash charges of $0.5 million, which included share-based compensation expense of $0.3 million and depreciation and amortization of $0.2 million. Net changes in our operating assets and liabilities for the three months ended March 31, 2018 consisted primarily of an increase in accounts receivable of $1.7 million primarily due to amounts earned for development milestones achieved under our Oxurion collaboration arrangement, a decrease of $1.1 million in deferred revenue, an increase of $0.8 million in research and development incentives receivable, an increase in other assets of $0.4 million and a $0.5 million decrease in accrued expenses and other current liabilities.

Net cash used in operating activities for the three months ended March 31, 2019 included our net loss of $6.5 million, net cash used by changes in our operating assets and liabilities of $2.4 million and non-cash charges of $3.7 million, which included share-based compensation expense of $0.3 million and depreciation and amortization of $0.2 million, as well as a changes in the fair value of our warrant liability of $3.2 million. Net changes in our operating assets and

liabilities for the three months ended March 31, 2019 consisted primarily of an increase of $1.7 million in research and development incentives receivable as well as a decrease in accounts receivable of $4.9 million primarily due to a receipt from AstraZeneca and a decrease in deferred revenue of $5.3 million due to the recognition of revenue related to the Bioverativ collaboration arrangement.

Net cash used in operating activities for the year ended December 31, 2017 included our net loss of $16.3 million, net cash provided by changes in our operating assets and liabilities of $13.1 million and net non-cash charges of $1.8 million, which included share-based compensation expense of $0.5 million and depreciation and amortization of $0.3 million, as well as a non-cash research and development expense of $0.9 million related to the issuance of warrants to purchase Series A convertible preferred shares to certain of our early investors and founders. Net changes in our operating assets and liabilities for the year ended December 31, 2017 consisted primarily of an increase in deferred revenue of $14.1 million primarily due to upfront payments received from our Bioverativ collaboration arrangement, an increase of $1.4 million in research and development incentives receivable, an increase in other assets of $1.0 million and a $1.3 million increase in accrued expenses and other current liabilities.

Net cash used in operating activities for the year ended December 31, 2018 included our net loss of $21.8 million, net cash used by changes in our operating assets and liabilities of $6.6 million and net non-cash charges of $2.4 million, which included share-based compensation expense of $1.0 million and depreciation and amortization of $0.7 million, as well as a changes in the fair value of our warrant liability of $0.7 million. Net changes in our operating assets and liabilities for the year ended December 31, 2018 consisted primarily of an increase of $3.6 million in research and development incentives receivable, an increase in accounts receivable of $0.4 million, an increase in prepaid expenses and other assets of $1.6 million, as well as a decrease in accounts payable of $0.2 million and a decrease deferred revenue of $3.9 million due to the recognition of revenue related to the Bioverativ collaboration arrangement. These amounts were offset by an increase in accrued expenses and other current liabilities of $2.6 million.

Investing Activities

During the three months ended March 31, 2018 and 2019, we used $0.3 million and $0.4 million, respectively, of cash in investing activities for purchases of property and equipment consisting primarily of laboratory equipment.

During the years ended December 31, 2017 and 2018, we used $1.1 million and $1.2 million, respectively, of cash in investing activities for purchases of property and equipment consisting primarily of laboratory equipment for new lease space obtained.

Financing Activities

During the three months ended March 31, 2018, the Company did not use or receive cash from financing activities.

During the three months ended March 31, 2019, net cash provided by financing activities was $34,000, consisting of net proceeds from the sale of our Series B2 convertible preferred shares issued in January 2019 of $1.3 million offset by payments of initial public offering costs of $1.3 million.

During the year ended December 31, 2017, net cash provided by financing activities was $57.9 million, consisting of $51.3 million and $6.6 million of net proceeds from the sale of our Series B1 convertible preferred shares issued in May 2017 and October 2017, respectively.

During the year ended December 31, 2018, net cash provided by financing activities was $25.4 million, consisting of net proceeds from the sale of our Series B2 convertible preferred shares issued in December 2018 offset by payments of initial public offering costs of $0.6 million.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates and as we:

- continue our development of our product candidates, including conducting future clinical trials of BT1718;
- progress the preclinical and clinical development for BT5528 and BT8009;
- seek to identify and develop additional product candidates;
- develop the necessary processes, controls and manufacturing data to obtain marketing approval for our product candidates and to support manufacturing of product to commercial scale;
- develop, maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- hire and retain additional personnel, such as non-clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, finance, commercial and scientific personnel;
- acquire or in-license other products and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base, including adding equipment and infrastructure to support our research and development; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs, any future commercialization efforts and our transition to operating as a public company following the completion of this offering.

In addition, if we obtain marketing approval for any product candidate that we identify and develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, and distribution are not the responsibility of our collaboration partners. Even if we are able to generate product sales, we may not become profitable. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and development programs or future commercialization efforts.

We expect that the net proceeds from this offering, together with our existing cash, will enable us to fund our operating expenses through for at least the next twelve months. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of product candidates and programs, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and

operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the scope, progress, results, and costs of drug discovery, preclinical development, laboratory testing, and clinical trials for the product candidates we may develop;
- our ability to enroll clinical trials in a timely manner and to quickly resolve any delays or clinical holds that may be imposed on our development programs;
- the costs associated with our manufacturing process development and evaluation of third-party manufacturers and suppliers;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of preparing and submitting marketing approvals for any of our product candidates that successfully complete clinical trials, and the costs of maintaining marketing authorization and related regulatory compliance for any products for which we obtain marketing approval;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive marketing approval;
- the terms of our current and any future license agreements and collaborations; and the extent to which we acquire or in-license other product candidates, technologies and intellectual property.
- the success of our collaborations with AstraZeneca, Oxurion and Bioverativ;
- our ability to establish and maintain additional collaborations on favorable terms, if at all; and
- the costs of operating as a public company.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, monetization transactions, government contracts or other strategic transactions. To the extent that we raise additional capital through the sale of equity, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights shareholder of our ADSs. If we raise additional funds through collaboration agreements, strategic alliances, licensing arrangements, monetization transactions, or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2018 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
	(in thousands)				
Operating lease commitments[1]	$ 3,187	$ 888	$ 1,816	$ 483	$ —
Total	$ 3,187	$ 888	$ 1,816	$ 483	$ —

(1) Amounts reflect minimum payments due for our office and laboratory space leases. We have one office lease in Cambridge, U.K. under an operating lease that expires in December 2021. We lease laboratory space in Lexington, Massachusetts under an operating lease that expires in December 2022.

We enter into various agreements with contract manufacturing organizations to provide clinical trial materials and with vendors for preclinical research studies, synthetic chemistry and other services for operating purposes. These payments are not included in the table of contractual obligations above since the contracts are generally cancelable at any time upon less than 90 days' prior written notice. We are not contractually able to terminate for convenience and avoid any and all future obligations to these vendors. Under such agreements, we are contractually obligated to make certain minimum payments to the vendors, with the payments in the event of a termination with less than 90 days' notice based on the timing of the termination and the exact terms of the agreement.

Legal Proceedings

From time to time, we may become involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business.

In September 2016, we filed a complaint in the District Court of the Hague against Pepscan Systems B.V. ("Pepscan") to contest the right of Pepscan to terminate a non-exclusive patent license agreement we entered into with Pepscan in 2009 and 2010. In response, Pepscan counterclaimed for injunctive relief and unquantified damages. We are vigorously prosecuting our claims and defending against those of Pepscan. We do not believe that a loss is probable or estimable at this time, and as such, we have not recorded a liability related to the Pepscan litigation as of December 31, 2017 and 2018. Should we not be successful in maintaining our rights to Pepscan's patent or in our alternative demand that the patent be invalidated, commercialization of our lead product could be delayed. As the Pepscan patent expires prior to the expected commercialization date of the product, we do not believe that the legal proceedings could have a material adverse effect on our business and operating results. We are unable to reasonably estimate a range of potential loss related to this matter at this time.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the

results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in greater detail in Note 2 to our consolidated financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Collaboration Revenues

Our revenues are generated primarily through collaborative arrangements and license agreements with pharmaceutical companies. The terms of these arrangements may include (i) performing research and development services using our bicyclic peptide screening platform with the goal of identifying compounds for further development and commercialization, (ii) options to obtain additional research and development services or licenses for additional targets, or to optimize product candidates, upon the payment of option fees, or (iii) the transfer of intellectual property rights (licenses).

The terms of these arrangements typically include payment to us of one or more of the following: non-refundable upfront license fees; payments for research and development services; fees upon the exercise of options to obtain additional services or licenses; payments based upon the achievement of defined collaboration objectives; future regulatory and sales-based milestone payments; and royalties on net sales of future products.

We adopted ASU 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASC 606") and all subsequent amendments using the full retrospective transition method for all periods presented. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services.

To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when, or as, we satisfy the performance obligations. We only apply the five-step model to contracts when it is probable that we will collect substantially all of the consideration we are entitled to in exchange for the goods or services it transfers to the customer. As part of the accounting for these arrangements, we must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Once a contract is determined to be within the scope of ASC 606, we assess the goods or services promised within the contract and determine those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations.

Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. The promised goods or services in our contracts with customers

primarily consist of license rights to our intellectual property for research and development, research and development services, and options to acquire additional research and development services or options to obtain additional licenses, such as a commercialization license for a potential product candidate. Promised goods or services are considered distinct when: (i) the customer can benefit from the good or service on its own or together with other readily available resources, and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, we consider factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own and whether the required expertise is readily available. In addition, we consider whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises.

We estimate the transaction price based on the amount of consideration we expect to receive for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, we evaluate the amount of the potential payments and the likelihood that the payments will be received. We utilize either the most likely amount method or expected value method to estimate variable consideration to include in the transaction price based on which method better predicts the amount of consideration expected to be received. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

After determining the transaction price, we allocate it to the identified performance obligations based on the estimated standalone selling prices. We must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. We utilize key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction, probabilities of technical and regulatory success and the estimated costs. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amounts we would expect to receive for each performance obligation.

We then recognize as revenue in the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time based on the use of an output or input method.

Licenses of Intellectual Property: If a license to our intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, we recognize revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are combined with other promises, such as research and development services and a research license, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby

periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

Research and Development Services: The promises under our collaboration agreements may include research and development services to be performed by us on behalf of the partner. Payments or reimbursements resulting from our research and development efforts are recognized as the services are performed and presented on a gross basis because we are the principal for such efforts.

Customer Options: We evaluate customer options to obtain additional items (i.e. additional license rights) for material rights, or options to acquire additional goods or services for free or at a discount. Optional future services that reflect their standalone selling prices do not provide the customer with a material right and, therefore, are not considered performance obligations and are accounted for as separate contracts. If optional future services reflect a significant or incremental discount, they are material rights, and are accounted for as performance obligations. We allocate the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments: Our collaboration agreements may include development and regulatory milestones. We evaluate whether the milestones are considered probable of being reached and estimate the amounts to be included in the transaction price using the most likely amount method. We evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as marketing approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, we re-evaluate the probability of achievement of such milestones and any related constraint, and if necessary, adjusts the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue and net loss in the period of adjustment.

Royalties: For sales-based royalties, including milestone payments based on the level of sales, we determine whether the sole or predominant item to which the royalties relate is a license. When the license is the sole or predominant item to which the sales-based royalty relates, we recognize revenue at the later of: (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any sales-based royalty revenue resulting from our collaboration agreements.

We receive payments from customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when our right to consideration is unconditional, such as when we have a contractual right to payment per the terms of the contract.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated

cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- vendors in connection with performing research activities on our behalf and conducting preclinical studies and clinical trials on our behalf;
- CMOs in connection with the production of preclinical and clinical trial materials;
- CROs, investigative sites or other service providers in connection with clinical trials;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing and development and distribution of preclinical and clinical supplies.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs, research institutions and vendors that supply, conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and actual results could differ from our estimates. Through December 31, 2018, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation

We are authorized to issue ordinary shares, as well as options and other securities exercisable for or convertible into ordinary shares, as incentives to our employees, consultants, and members of our board of directors. To the extent such incentives are in the form of share options, the options may have been granted pursuant bilateral EMI option award agreements in the form approved by the board of directors. Such agreements provide for the grant of potentially tax-favored Enterprise Management Incentive, or EMI, options, to our U.K. employees, directors and consultants. Options issued pursuant to such agreements have an exercise price of £0.01 per share. The exercise price for share options granted to U.S. employees have an exercise price that is not less than the fair value of ordinary shares as determined by the board of directors as of the date of grant. Exercise prices of our options to subscribe for ordinary shares and restricted share are in British Pound Sterling.

We measure share-based awards granted to employees and directors based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. We record the expense for awards with only service-based vesting conditions using the straight-line method and account for forfeitures as they occur.

We have granted awards that include both a service condition, that vest over time, and a performance condition, that will accelerate vesting upon the achievement of a specified collaboration revenue threshold. For equity awards that contain both performance and service conditions, we recognize share-based compensation expense using an accelerated attribution model over the requisite service period when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance condition as of the reporting date.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation — Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07") to simplify the accounting for share-based payments to nonemployees by aligning it with the accounting share-based payments to employees, with certain exceptions. We adopted the new standard on January 1, 2019. Prior to the adoption, compensation expense for share-based awards granted to non-employee consultants was recognized over the period during which services are rendered by such consultants until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards was remeasured using the then-current fair value of our ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model, as applicable. Under the new guidance, the measurement date for non-employee awards is the date of grant. The compensation expense is then recognized over the requisite service period, which is the vesting period of the respective award, without subsequent changes in the fair value of the award.

The fair value of each restricted ordinary share award is based on the fair value of our ordinary shares, less any applicable purchase price.

The fair value of each share option is estimated using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the fair value of ordinary shares, the expected share price volatility, the expected term of the award, the risk-free interest rate, and expected dividends. See Note 9 to our consolidated financial statements appearing at the end of this prospectus for more information.

We classify share-based compensation expense in our consolidated statements of operations in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Determination of the Fair Value of Ordinary Shares

Given the absence of an active market for our ordinary shares, the board of directors determined the fair value of the ordinary shares based on input from management, which utilized an independent valuation of our enterprise value, determined utilizing an analytical valuation model. The third party valuation reports performed utilized various valuation methodologies in accordance with the framework of the *American Institute of Certified Public Accountants' Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its ordinary shares. Each valuation methodology includes estimates and assumptions that require judgment. These estimates and assumptions include a number of objective and subjective factors in determining the value of our ordinary shares at each grant date, including the following factors:

- prices paid for our convertible preferred shares, which we had sold to outside investors in arm's-length transactions, and the rights, preferences, and privileges of our convertible preferred shares and ordinary shares;
- valuations performed by an independent valuation specialist;
- our stage of development and our business strategy,

- the progress of our research and development programs, including the status of preclinical studies and planned clinical trials for our product candidates;
- the fact that the grants of share-based awards involved illiquid securities in a private company;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results
- the likelihood of achieving a liquidity event for the underlying ordinary shares; and
- external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;

The analytical valuation models through March 31, 2019 employed an Option Pricing Model, or OPM, and a hybrid approach based on an OPM method and the Probability Weighted Expected Return Method, or PWERM.

OPM

The OPM treats ordinary and convertible preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, securities such as ordinary shares have value only if the funds available for distribution to shareholders exceeded the value of the convertible preferred shares liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. The ordinary shares are modeled as a call option on the underlying equity value at a predetermined exercise price. In this model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular call option, a comparison with a per share price. Thus, ordinary shares are considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the convertible preferred share liquidation preference is paid.

The OPM uses the Black-Scholes option-pricing model to price the call options. This model defines the securities' fair values as functions of the current fair value of a company and uses assumptions, such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities. The aggregate value of the ordinary shares derived from the OPM is then divided by the number of ordinary shares outstanding to arrive at the per share value.

We used the OPM back-solve approach to estimate enterprise value under the OPM. The OPM back-solve approach uses the OPM to derive an implied equity value for one type of a company's equity securities from a contemporaneous sale transaction involving another type of the company's equity securities. For the OPM, we based our assumed volatility factor on the historical trading volatility of our publicly traded peer companies. At each valuation date, we determined the appropriate volatility to be used, considering such factors as our expected time to a liquidity event and our stage of development.

To derive the fair value of our ordinary shares using the OPM, we calculated the proceeds to our ordinary shareholders based on the preferences and priorities of our convertible preferred shares and ordinary shares. We then applied a discount for lack of marketability to the ordinary shares to account for the lack of access to an active public market.

Hybrid method

The hybrid method is a hybrid between the PWERM and OPM, estimating the probability-weighted value across multiple scenarios, but also using the OPM to estimate the allocation of value within one of more of the scenarios. The hybrid method can be a useful alternative to

explicitly modeling all PWERM scenarios in situations when the company has transparency into one or more near term exits, but is unsure what will occur if the current plans fall through. The PWERM is a scenario-based methodology that estimates the fair value of securities based upon an analysis of future values for the company, assuming various outcomes. The securities' value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each share class. The future value under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the ordinary shares.

Valuations method

Our retrospective valuation of our ordinary shares as of September 30, 2017 were prepared using the OPM back-solve approach.

Our retrospective valuations of our ordinary shares as of May 31, 2018 and September 30, 2018, as well as our contemporaneous valuation on December 31, 2018 were prepared using the OPM method, which incorporated probability weighting of sale and IPO outcomes, because of an increase in the likelihood of an IPO.

Our contemporaneous valuation of our ordinary shares as of March 31, 2019 was prepared using the hybrid approach based on an OPM method and the PWERM approach.

These third-party valuations performed resulted in valuations of our ordinary shares of $2.60 per share as of September 30, 2017, $2.64 per share on May 31, 2018, $3.41 per share on September 30, 2018, $4.81 per share on December 31, 2018, and $8.29 per share on March 31, 2019, as converted to dollars using the exchange rate on the respective valuation dates.

The assumptions underlying these valuations represented our board of directors' best estimates at the time they were made, which involve inherent uncertainties and the application of the judgment of our board of directors. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our share-based compensation expense could be materially different.

Once a public trading market for our ordinary shares has been established in connection with the completion of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our ordinary shares in connection with our accounting for granted share options and other such awards we may grant, as the fair value of our ordinary shares will be determined based on the quoted market price of our ordinary shares.

Options and Restricted Shares Granted

The following table sets forth, by grant date, the number of shares subject to options granted since January 1, 2018, the per share exercise price of the options, the fair value per ordinary share on each grant date, and the per share estimated fair value of the options:

Grant Date	Type of Award	Number of Shares	Purchase or Exercise Price Per Share[1][4]	Fair Value Per Ordinary Share on Grant Date[4] (as restated)	Per Share Estimated Fair Value on Grant Date[3][4] (as restated)
February 1, 2018[2]	Options	18,719	$ 1.81	$ 2.53	$ 1.81
February 8, 2018[2]	Restricted Shares	9,127	$ 0.01	$ 2.53	$ 2.53
September 18, 2018[2]	Options	52,156	$ 1.88	$ 2.59	$ 1.90
November 30, 2018[2]	Options	22,864	$ 2.59	$ 3.40	$ 2.53
December 1, 2018[2]	Options	5,001	$ 2.59	$ 3.40	$ 2.53
December 17, 2018[2]	Options	24,004	$ 3.54	$ 4.92	$ 3.70
December 17, 2018[2]	Options	160,239	$ 0.01	$ 4.92	$ 4.91
December 17, 2018[2]	Restricted Shares	19,234	$ 0.01	$ 4.92	$ 4.91
January 31, 2019	Options	122,316	$ 3.54	$ 4.92	$ 3.68
April 25, 2019	Options	375,823	$ 8.30	$ 8.30	$ 5.71

(1) Represents the determination by our board of directors of the fair value of our ordinary shares on the date of grant, taking into consideration the various objective and subjective factors described below.

(2) The fair value of ordinary shares at the grant date was adjusted in connection with a retrospective fair value assessment for financial reporting purposes.

(3) For purposes of recording share-based compensation for grants of options to a non-employee, we measure the fair value of the award on the service completion date (vesting date). At the end of each reporting period prior to completion of the services, we remeasure the value of any unvested portion of the award based on the then-current fair value of the award and adjust the expense accordingly. The amount in this column reflects only the grant-date fair value of the award.

(4) The exercise prices per the respective share options and the subscription price of restricted shares are in pounds sterling. The amounts in this table are translated to U.S. Dollars at the rate of $1.303 to £1.00, which was the noon buying rate of the Federal Reserve Bank of New York on March 29, 2019, the last business day of the three months ended March 31, 2019.

On December 17, 2018, each of the U.K. employees that were holders of share options granted prior to December 2017, each with an exercise price of £0.01 per share, surrendered all of their issued share options that had not lapsed or been exercised. Thereafter, such persons: (a) subscribed for ordinary shares equal to such number of ordinary shares as were vested under their surrendered option agreement at a subscription price of £0.01 per ordinary share; and (b) were granted options to subscribe for ordinary shares equal to such number of ordinary shares as were unvested under their surrendered option agreement at a subscription price of £0.01 per ordinary share, and with identical vesting terms as the original awards. In conjunction with the surrender of 340,728 vested share options, we issued 340,728 ordinary shares. This surrender and subsequent issuance only impacted employees in the U.K. We evaluated the surrender of share options and issuance of vested ordinary shares and unvested share options as a modification in accordance with ASU 2017-09. The modification did not have any accounting impact as there were no changes in the fair value, vesting conditions, or the classification of the awards (as equity or liability) in conjunction with the surrender of share options and issuance of vested ordinary shares and unvested share options. As such, the grant of options to subscribe for ordinary shares equal to such number of ordinary shares as were unvested under their surrendered option agreement at a subscription price of £0.01 per ordinary share, and with identical vesting terms as the original awards is not reflected in the table above.

For the years ended December 31, 2017 and 2018, we recorded share-based compensation expense for share options and restricted shares granted of $0.5 million and $1.0 million, respectively. For the three months ended March 31, 2018 and 2019, we recorded share-based compensation expense for share options and restricted shares granted of $0.3 million and $0.3 million, respectively. Expense for non-employee consultants was immaterial in all periods. As of March 31, 2019, total unrecognized compensation expense related to the unvested employee and director share-based awards was $1.6 million, which is expected to be recognized over a weighted average period of 3.2 years. As of March 31, 2019, total unrecognized compensation cost related to the unvested employee and director restricted share awards was $0.1 million, which is expected to be recognized over a weighted average period of 1.8 years. We expect the impact of our share-based compensation expense for restricted shares and share options granted to employees and non-employees to increase in future periods due to the potential increases in the value of our ordinary shares and headcount.

Income Taxes

We account for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in our tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. We assess the likelihood that our deferred tax assets will be recovered in the future and, to the extent we believe, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies. See Note 11 to our consolidated financial statements appearing at the end of this prospectus for additional information.

We are subject to corporate taxation in the United Kingdom and the United States. The calculation of our tax provision involves the application of both U.K. and U.S. tax law and requires judgement and estimates.

We account for uncertainty in income taxes in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed as the amount of benefit to recognize in the consolidated financial statements. The amount of benefits that may be used is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes included the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate, as well as the related net interest and penalties.

We receive reimbursements of certain research and development expenditures, through our subsidiaries in the United Kingdom, as part of a United Kingdom government's research and development tax reliefs program. Under the program, a percentage of qualifying research and development expenses incurred by the Company's subsidiaries in the United Kingdom are reimbursed up to 14.5% of the surrendable losses. We assess our research and development activities and expenditures to determine which activities and expenditures are likely to be eligible under the research and development incentive program described above. At each period end, we estimate the reimbursement available to the Company based on available information at the time.

We recognize income from the research and development incentives when the relevant expenditure has been incurred, the associated conditions have been satisfied and there is reasonable assurance that the reimbursement will be received. We record these research and development incentives as a reduction to research and development expenses in the statements of operations and comprehensive loss, as the research and development tax credits are not dependent on us generating future taxable income, our ongoing tax status, or tax position. The refund is denominated in pounds sterling and, therefore, the receivable is remeasured into U.S. dollars as of each reporting date. The research and development incentives receivable represent an amount due in connection with the above program. We recorded a reduction to research and development expense of $2.9 million and $5.9 million during the years ended December 31, 2017 and 2018, respectively. We recorded a reduction to research and development expense of $0.8 million and $1.7 million during the three months ended March 31, 2018 and 2019, respectively.

Quantitative and Qualitative Disclosures About Market Risks

Interest Rate Sensitivity

As of March 31, 2019, we had cash of $59.4 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. Our surplus cash has been invested in interest-bearing savings accounts. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

As of March 31, 2019, we had no debt outstanding and are therefore not subject to interest rate risk related to debt.

Foreign Currency Exchange Risk

The functional currency of Bicycle Therapeutics Limited and its wholly owned non-U.S. subsidiaries, BicycleTx Limited and BicycleRD Limited, is the British Pound Sterling and the consolidated financial statements are presented in United States dollars, USD. The functional currency of Bicycle Therapeutics Inc. is the United States dollar. The functional currency is the currency of the primary economic environment in which an entity's operations are conducted. The functional currency of the Company's subsidiaries is the same as the local currency.

Monetary assets and liabilities denominated in currencies other than the functional currency are remeasured into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are remeasured into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net loss for the respective periods. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in general and administrative expense in the consolidated statements of operations and comprehensive loss as incurred. We recorded a foreign exchange loss of $0.6 million and a foreign exchange gain of $0.3 million for the years ended December 31, 2017 and 2018, respectively. We recorded foreign exchange losses of $0.3 million and $0.3 million for the three months ended March 31, 2018 and 2019, respectively. These foreign currency transaction gains and losses are included in other expense in our consolidated statements of operations and comprehensive loss.

For financial reporting purposes, our consolidated financial statements have been translated into U.S. dollars. We translate the assets and liabilities of Bicycle Therapeutics Limited, BicycleTx

Limited and BicycleRD Limited into USD at the exchange rate in effect on the balance sheet date. Revenues and expenses are translated at the average exchange rate in effect during the period and shareholders' (deficit) equity amounts are translated based on historical exchange rates as of the date of each transaction. Translation adjustments are not included in determining net income (loss) but are included in our foreign exchange adjustment included in the consolidated statements of convertible preferred shares and shareholders' (deficit) equity as a component of accumulated other comprehensive income (loss).

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future.

Emerging Growth Company Status

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

In addition, we intend to rely on the other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, we are entitled to rely on certain exemptions as an "emerging growth company," we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b), (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that has or may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis), and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation. These exemptions will apply for a period of five years following the completion of this offering or until we no longer meet the requirements of being an emerging growth company, whichever is earlier. We would cease to be an emerging growth company if we have more than $1.07 billion in annual revenue, we have more than $700.0 million in market value of our share held by non-affiliates (and we have been a public company for at least 12 months and have filed one annual report on Form 10-K), or we issue more than $1.0 billion of non-convertible debt securities over a three-year period.

Off-balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

BUSINESS

We are a clinical-stage biopharmaceutical company developing a novel class of medicines, which we refer to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint is designed to confer high affinity and selectivity and the relatively large surface area presented by the molecule allows targets to be drugged that have historically been intractable to non-biological approaches. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic, or PK, properties of a small molecule. *Bicycles* are excreted by the kidney rather than the liver and have shown no signs of immunogenicity to date, which we believe together support a favorable toxicological profile.

We have a novel and proprietary phage display screening platform which we use to identify *Bicycles* in an efficient manner. The platform initially displays linear peptides on the surface of engineered bacteriophages, or phages, before "on-phage" cyclization with a range of small molecule scaffolds which can confer differentiated physicochemical and structural properties. Our platform encodes quadrillions of potential *Bicycles* which can be screened to identify molecules for optimization to potential product candidates. We have used this powerful screening technology to identify our current portfolio of candidates in oncology and intend to use it in conjunction with our collaborators to seek to develop additional future candidates across a range of other disease areas.

Our initial internal programs are focused on oncology indications with high unmet medical need. Our lead product candidate, BT1718, is a *Bicycle* Toxin Conjugate, or BTC. This *Bicycle* is being developed to target tumors that express Membrane Type 1 matrix metalloprotease, or MT1-MMP. The *Bicycle* is chemically attached to a toxin that when administered is cleaved from the *Bicycle* and kills the tumor cells. BT1718 is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial in collaboration with, and fully funded by, the Centre for Drug Development of Cancer Research UK, or CRUK. We expect to report preliminary data from the Phase I part of this clinical trial in the second half of 2019. We are also developing BT5528 and BT8009, which are BTCs targeting Ephrin type-A receptor 2, or EphA2, and Nectin-4, respectively, for oncology indications. We are currently conducting Investigational New Drug application, or IND, -enabling activities for BT5528 and BT8009. Our discovery pipeline in oncology includes *Bicycle*-targeted innate immune activators as well as T-cell modulators.

Beyond oncology, we are collaborating with biopharmaceutical companies and organizations in therapeutic areas where we believe our proprietary *Bicycle* screening platform can identify therapies to treat diseases with significant unmet medical need. Our partnered programs outside of oncology include collaborations for anti-bacterial, cardiovascular, hematology, ophthalmology and respiratory indications.

The following table summarizes key information about our programs:

Product/Target	Interest	Collaborations	Stage
			Preclinical / Phase I / Phase II / Phase III
Bicycle Toxin Conjugates			
BT1718 (MT1-MMP)	Oncology (focused on MMT1-MMP expression)	Cancer Research UK	
BT5528 (EphA2)	Oncology (focused on EphA2 expression)		
BT8009 (Nectin-4)	Oncology (focused on Nectin-4 expression)		
Beyond Oncology			
THR-149 (Plasma Kallikrein Inhibitor *Bicycle*)	Ophthalmology	Oxurion	

We were founded in 2009 based on innovative science conducted by Sir Greg Winter and Professor Christian Heinis. Sir Greg Winter is a pioneer in monoclonal antibodies and, in 2018, was awarded a Nobel prize in chemistry for the invention of the technology underpinning our proprietary phage display screening platform that we use to identify *Bicycles*. Since our founding, we have generated substantial intellectual property, including three patent families directed to novel scaffolds, 11 patent families directed to our platform technology, 63 patent families directed to bicyclic peptides and related conjugates, and six patent families directed to clinical indications and other properties of development assets. The work we have conducted in developing *Bicycles* and our proprietary screening platform have created substantial know-how that we believe provides us with a competitive advantage.

Our management team includes veterans in drug development with executive experience at leading pharmaceutical companies including GlaxoSmithKline, Novartis and Pfizer. Our board of directors and scientific advisory board include industry experts and seasoned investors, with extensive experience in immuno-oncology. We are supported by prominent healthcare-focused investment funds, including Ahren Innovation Capital, Atlas Venture Fund, Cambridge Innovation Capital, Longwood Fund, Novartis Venture Fund, S.R. One, Limited, SV Health Investors, Tybourne Capital (HK) Management Limited and Vertex HC Ventures.

Our Strategy

Our mission is to become a leading biopharmaceutical company by pioneering *Bicycles* as a novel therapeutic modality to treat diseases that are inadequately addressed with existing treatment modalities. Specifically, we seek to execute on the following strategy to maximize the value of our novel technology and pipeline:

- ***Advance our lead product candidate, BT1718, through clinical development.*** BT1718 is being investigated in an ongoing Phase I/IIa clinical trial sponsored by CRUK. We expect to report preliminary data from the Phase I part of this clinical trial in the second half of 2019. We intend to advance development of this candidate aggressively across oncology indications in which the target MT1-MMP is expressed.

- ***Advance our other Bicycle Toxin Conjugate programs into clinical development.*** We intend to progress our IND-enabling activities for BT5528 and BT8009 to advance these programs into clinical development for oncology indications. Based on promising observations from our preclinical models, we believe EphA2 and Nectin-4 are attractive targets for cytotoxin delivery and that *Bicycles* provide a promising delivery modality.

- ***Pursue clinical development of our discovery programs.*** We intend to continue our ongoing discovery activities to screen and select promising candidates for oncology

indications. For example, our discovery pipeline includes T-cell modulators, from which we expect to identify a development candidate. In addition, we are also developing *Bicycle*-targeted innate immune activators.

- ***Leverage our powerful proprietary screening platform and novel Bicycle modality to grow our pipeline.*** Our novel and proprietary phage display screening platform allows us to rapidly and efficiently identify potential candidates for development. We can incorporate a wide range of small molecule scaffolds into *Bicycles* to increase diversity and confer differentiated physicochemical and structural properties. We have used our powerful *Bicycle* screening platform to identify our current pipeline of promising BTCs, innate immune activators and T-cell modulators, and intend to use it to develop a broader pipeline of diverse product candidates.

- ***Collaborate strategically with leading organizations to access enabling technology and expertise in order to expand the application of our novel Bicycle modality to indications beyond oncology.*** We are collaborating with leading biopharmaceutical companies and organizations to apply our novel *Bicycle* modality to other disease areas, including neurological, anti-bacterial, cardiovascular, hematological, ophthalmological and respiratory indications. We may opportunistically enter into additional collaborations in the future to apply our technology to areas of unmet medical need.

- ***If approved, maximize the commercial potential of our product candidates by either establishing our own sales and marketing infrastructure or doing so through collaborations with others.*** Subject to receiving marketing approval, we intend to pursue the commercialization of our product candidates either by building internal sales and marketing capabilities or doing so through opportunistic collaborations with others.

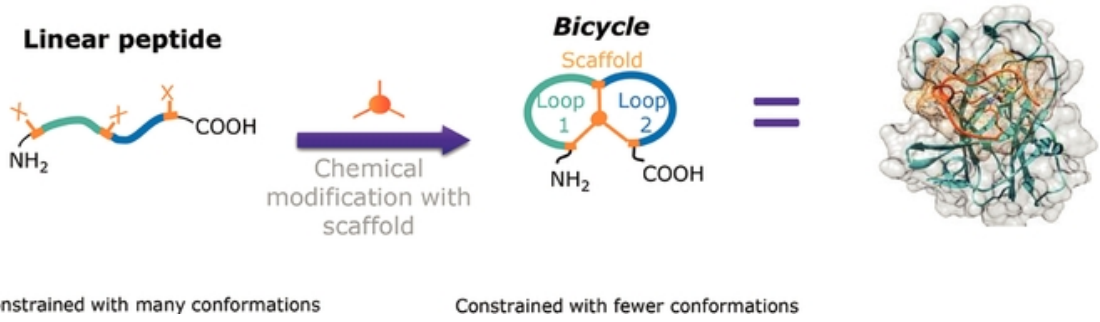
The *Bicycle* Opportunity

Introduction to Bicycles

Bicycles are fully synthetic, short peptides consisting of nine to 15 amino acids constrained to form two loops which stabilize the structural geometry of the peptide and facilitate target binding with high affinity and selectivity. *Bicycles* represent a unique therapeutic class, combining the pharmacological properties normally associated with a biologic with the manufacturing and PK advantages of a small molecule, with no signs of immunogenicity observed to date.

Drugs must bind to target proteins with high affinity and selectivity to achieve a therapeutic effect, while minimizing undesired effects on other proteins and physiological functions. Peptides exist in a number of folded states, only a few of which are able to bind to target proteins, and a key challenge for peptide therapeutics is designing structures that achieve these goals. We have designed our molecules to be highly constrained by linking a chemical connector compound, also known as a scaffold, to particular amino acids in the peptide chain. The resulting cyclized molecule, which we refer to as a *Bicycle*, is locked in the preferred state to bind to the target proteins.

Schematic of the Creation of a Cyclized Molecule Resulting in a Bicycle



We have expanded the diversity of the chemical space we can cover from approximately 10^{13} potential molecules in 2009 to 10^{17} today. We have applied our novel *Bicycle* modality to a growing range of targets, from a single target in 2009 to more than 90 today. We can create a wide range of *Bicycles* by varying four parameters:

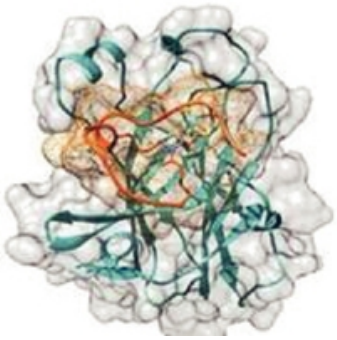
- the number of amino acids in the two loops;
- the amino acid composition at each position;
- the symmetry of the two loops; and
- the small molecule scaffold used to cyclize the *Bicycle*.

Properties of Bicycles as Therapeutic Agents

Bicycles have a large surface area available for target binding, which is designed to allow for high affinity and selectivity to the designated target. As short sequences of amino acids, or peptides, they have a low molecular weight, typically ranging from 1.5 kDa to 2.0 kDa. *Bicycles* have a readily adjustable PK profile with good plasma stability and rapid distribution from the vasculature into the extracellular space. This PK profile enables rapid tissue penetration and a renal route of elimination that minimizes liver exposure. Toxicity issues are observed with small molecules that are metabolized and eliminated by the liver. *Bicycle* peptides, by contrast, are not subject to metabolism or elimination by the liver but are metabolized in the peripheral circulation or kidney with subsequent rapid excretion in the urine. Consequently, by increasing excretion in urine, the liver exposure is minimized and the risk of liver toxicity is reduced. The modular nature of *Bicycles* allows us to optimize therapeutic molecules for specific targets. To date, we have observed no signs of immunogenicity.

Compared to biologics, *Bicycles* have a lower cost of production and a simpler manufacturing process, and are recognized by regulatory authorities as small molecule new chemical entities. *Bicycles* can be readily identified to drug a wide spectrum of targets and target classes, including many that have so far been undruggable with small molecules, such as protein-protein interactions. Our novel and proprietary screening platform allows us to screen *Bicycles* against molecular targets rapidly and efficiently, affording potentially reduced timelines and costs compared to other high-throughput screening approaches. Leveraging our platform, we can rapidly and efficiently identify a compound for development in as few as six months with the historical average time being 12 months after a target has been selected.

The figure shown below is the x-ray diffraction crystal structure of a bicyclic peptide binding to EphA2 ligand-binding domain.



The selectivity of the *Bicycle* for EphA2 as compared to other Eph family members with similar structure and sequence homology was determined using surface plasmon resonance. No binding was observed to any of the family members tested up to the maximum concentration feasible, limited by concentration of protein sample. This illustrates the high selectivity that we expect of *Bicycle*/target interaction.

Ligand-binding domain	% identity to EphA2	Binding affinity (SPR K_D nM)
EphA2	100	1.2
EphA1	54	>5000
EphA3	58	>5000
EphA4	55	>5000
EphA5	56	>25000
EphA6	56	>20000
EphA7	56	>20000
EphB4	39	>20000

Properties of Bicycles May Translate into Potential Therapeutic and Other Advantages

Bicycle Property	Importance	Strategic Potential
Bicyclic structure	• Conformational constraint to reduce rotational freedom	• High affinity to designated target • Increased selectivity to designated target
	• Stable 3D structure	• Ability to adopt structures found in native ligands • Ability to generate diverse libraries covering a wide chemical space • No immunogenicity observed to date • Novel structures suitable for patent protection
Small size	• Rapid and extensive extravascular permeability	• Rapid penetration into tissue (e.g. tumor) • Controllable systemic half-life allows the creation of short or long acting molecules
	• Renal elimination	• Bypass of liver metabolism/processing to reduce liver and gastrointestinal toxicity
	• High payload to *Bicycle* ratio	• Low tendency for aggregation • Ease of formulation • High toxin delivery
Large molecular footprint	• Ability to target and disrupt protein-protein interactions	• Ability to bind to target classes usually intractable to small molecule approaches • High selectivity • High affinity
Fully synthetic manufacturing	• Scalable and controllable manufacturing through well established procedures	• Reduced cost of goods compared to biologics • Defined product composition • Multiple suppliers for manufacturing
Ability to conjugate	• Versatility to easily combine with *Bicycles*/modalities without affecting properties • Potential to create multivalent molecules, e.g. bifunctionals, other trifunctionals	• Ability to quickly and efficiently generate a range of drug candidates from small number of *Bicycles*

Comparison of Bicycles to Other Common Classes of Therapeutics

	Bicycle	Antibody	ScFv (fragment)	Peptide	Small molecule
Molecular Weight (kDa)	~1.5-2	~150	~28	~1-5	~<0.8
Extracellular volume	Whole body	Low (vascular)	Intermediate	Whole body	Typically whole body
Half life	Minutes to hours (adjustable). Days possible*	Days to weeks	Minutes to days*	Minutes to hours	Hours (tunable)
Clearance	Renal	Hepatic	Renal, hepatic	Renal, hepatic	Renal, hepatic
Tumor penetrance	High	Low (outer rim only)	Low (poor exposure)	Medium to high	High
Target classes	All tested successful	Many, but can be restricted due to large size	Many, but can be restricted due to large size	Many	Limited
Selectivity	High	High	High	Medium	Poor
Modularity	High	Low	Low	High	Low
Synthesis	Simple	Complex biologic	Complex biologic	Simple	Simple
Immunogenicity	None detected to date	Possible	Frequent	Possible	None

*Requires use of extension technology

Our Proprietary *Bicycle* Screening Platform

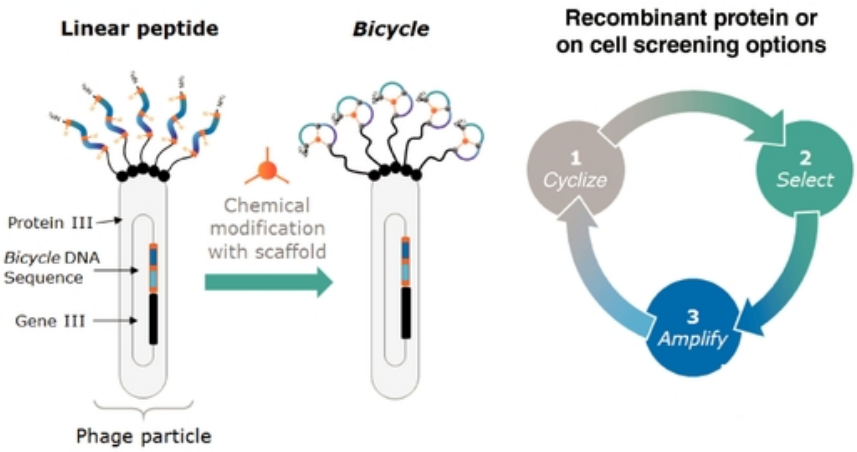
We utilize our novel and proprietary phage display screening platform to identify *Bicycles* that are potentially useful in medicine. We have used this technology to identify our current pipeline, and intend to leverage it to develop a broader portfolio of product candidates to address unmet medical needs across a wide range of diseases.

Phages are bacteria-infecting viruses consisting of genetic material wrapped in a protein coat. Phages can be harnessed to identify *Bicycles* by splicing DNA into the genome of a phage so that the linear peptides that encode *Bicycles* are presented on the surface of the phage. Our founder Sir Greg Winter, a pioneer in phage display, applied this technology and added a cyclization step that

forms *Bicycles* from these linear peptides. This technology underpins our novel and proprietary screening platform.

Our screening process self-selects for *Bicycles* that are amenable to attachment, commonly referred to as conjugation, to other molecular payloads such as cytotoxins, innate immune activators or other *Bicycles*. *Bicycles* can be linked together with synthetic ease to create complex molecules with combinatorial pharmacology. Alternatively, *Bicycles* in the form of multimers can also be used as standalone therapeutics, such as those that we are exploring in our T-cell modulator program. We believe that the flexibility of our *Bicycles* and our powerful screening platform allow new therapeutics to be rapidly conceived and reduced to practice to potentially serve diverse therapeutic applications across a wide range of indications.

Schematic of our Proprietary Bicycle Screening Process



We have optimized our proprietary *Bicycle* screening platform, enabling the technique to be applied to a diverse range of over 90 challenging targets to date, successfully identifying *Bicycles* for over 80% of these targets, some of which are intractable to small molecules. During these screens, *Bicycles* with diverse pharmacologies were identified, including enzyme inhibitors, receptor antagonists, agonists (partial, full and supra) and neutral site binders. Neutral site binders often bind to entirely novel sites on target proteins, previously undescribed in the scientific literature. These binders can be useful when conjugated with therapeutic payloads since they allow antigen-targeted payload delivery without impacting target function.

Our Product Candidates

Our portfolio of internal product candidates is directed to oncology applications where we believe they have the potential to treat a broad spectrum of cancers. We are collaborating with biopharmaceutical companies and organizations in other therapeutic areas, where we believe our proprietary *Bicycle* screening platform can identify therapies to treat diseases with significant unmet medical need.

Our Pipeline

The following table summarizes key information about our pipeline programs.

Program	Interest	Stage	Status
Oncology ***Bicycle* Toxin Conjugates**			
BT1718	• High MT1-MMP expressing tumors (e.g., breast cancer, lung cancer, sarcoma, gastric cancer, ovarian cancer, endometrial cancer, bladder cancer, esophageal cancer)	• Phase I/IIa	• Ongoing Phase I/IIa clinical trial in collaboration with CRUK. Preliminary clinical data from Phase I part of the trial expected in the second half of 2019
BT5528	• High EphA2 expressing tumors (e.g., lung cancer, breast cancer, bladder cancer, gastric cancer, ovarian cancer, esophageal cancer, pancreatic cancer)	• Preclinical	• IND-enabling activities in process
BT8009	• High Nectin-4 expressing tumors (e.g. breast cancer, bladder cancer, pancreatic cancer, lung cancer, gastric cancer, ovarian cancer)	• Preclinical	• IND-enabling activities in process
***Bicycle*-Targeted**			
Systemically-Delivered Activators	• Oncology	• Discovery	• Discovery activities in process
T-Cell Modulators			
CD137	• Oncology	• Discovery	• Discovery activities in process
Beyond Oncology			
THR-149 (Plasma Kallikrein Inhibitor)	• Ophthalmology	• Phase I	• Collaborating with Oxurion
Inhaled	• Respiratory	• Discovery	• Collaborating with AstraZeneca
Cardiovascular	• Cardiovascular	• Discovery	• Collaborating with AstraZeneca
Hematology	• Hemophilia	• Discovery	• Collaborating with Bioverativ
Novel anti-bacterials	• Anti-bacterials	• Discovery	• Collaborating with Innovate UK
Neurological	• Dementia	• Discovery	• Collaborating with Dementia Defense Fund

Our Oncology Programs

We believe *Bicycles* are an ideal vehicle to deliver small molecule payloads to tumors, both as potent cytotoxins in the case of BTCs, as well as small molecule agonists of the immune system in the case of our *Bicycle*-targeted immune activators. We believe that *Bicycle* conjugates can offer improved performance as compared to antibody-mediated delivery.

In addition to their use as drug conjugates, *Bicycles* can also be configured for use as standalone therapeutics in the form of multimers. We have identified *Bicycles* that have been observed to directly interact with CD137, a key immune cell co-stimulatory molecule. We believe our CD137-targeting *Bicycles* may overcome limitations inherent in antibody-mediated approaches and have the potential to be converted into simple "bi-specific" immune cell-engaging *Bicycle* molecules.

Bicycle Toxin Conjugates

Within our BTC programs, we are developing BT1718 (carrying a DM1 cytotoxin payload), which is designed to target MT1-MMP expressing tumors. BT1718 is currently being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial that is being conducted in collaboration with CRUK. We expect to receive preliminary data from the Phase I part of this clinical trial in the second half of 2019. We are also conducting IND-enabling activities for BT5528 and BT8009 (carrying a monomethyl auristatin E, or MMAE cytotoxin payload), targeting EphA2 and Nectin-4, respectively. Studies have demonstrated that MT1-MMP, EphA2 and Nectin-4 are overexpressed in many cancer cell types with high unmet medical needs, including lung cancer, breast, gastric, endometrial, sarcoma pancreatic, bladder, ovarian, esophageal and other cancers. Studies have also shown that tumor overexpression in each of these targets has been associated with poor prognosis in specific cancers. We therefore believe our BTC candidates may address a wide range of cancer types with significant unmet medical need.

Background

The discovery of monoclonal antibodies enabled the development of antibody drug conjugates, or ADCs. ADCs link antibodies that target tumor-associated antigens to potent cytotoxins through a process known as conjugation. ADCs are designed to selectively and potently destroy cancer cells by combining the targeting capability of antibodies with the cancer-killing ability of cytotoxins. Despite the growing use of ADCs in treating cancer and high interest in ADC development programs, we believe there are significant challenges to ADCs. The large molecular size of the antibody impairs the penetration of ADCs into tumors. ADCs are generally required to internalize into tumor cells after binding to internalizing tumor antigens to the surface. Finally, the relatively long systemic exposure and subsequent liver clearance generally associated with ADCs result in dose-limiting toxicities such as hematological, liver and gastrointestinal toxicities, and neuropathies.

Properties of Bicycle Toxin Conjugates

We believe the properties of our BTCs may address the challenges associated with ADCs and therefore that our approach has the potential to offer substantial benefits, including:

- ***Extensive and rapid tumor penetration.*** *Bicycles* have been observed in our preclinical studies to penetrate tumors more rapidly and exhibited increased penetration to poorly perfused regions of the tumor when compared to a comparator antibody. Preliminary clinical data from three post-dose tumor biopsies in patients from our ongoing Phase I trial of BT1718 is consistent with preclinical observations that the cytotoxin payload DM1 rapidly penetrated the tumor.

- ***Retention in tumors.*** In preclinical studies a tumor antigen targeting *Bicycle* was observed to be retained in the tumor or at least 120 hours after dosing. Preliminary clinical data observed to date from our ongoing Phase I trial of BT1718 is consistent with preclinical observations of post-dose tumor retention. Biopsies taken from three patients following the infusion of BT1718 exhibited retention of the cytotoxin payload DM1 in the tumor at concentrations consistent with preclinical data.

- ***Short systemic half-life and renal elimination****. Bicycles* have been observed in clinical and preclinical studies to have a short systemic half-life of approximately 20-30 minutes. Due to their small size, *Bicycles* are able to exit the tissue rapidly and are excreted through the kidneys rather than the liver, which we expect will support a favorable toxicity profile.

- ***No requirement for internalization.*** Unlike ADCs, which require cellular internalization for activity, BTCs do not require internalization into the cell, and therefore potentially can target a wider range of tumor antigens.

- ***Access to non-expressing tumor cells.*** The toxin in our BTCs is liberated in the extracellular space, enabling cell-killing adjacent cells that do not express the specific target through a toxin bystander effect. In our preclinical studies, we observed activity for BTCs even in tumors that were heterogeneous for target expression.

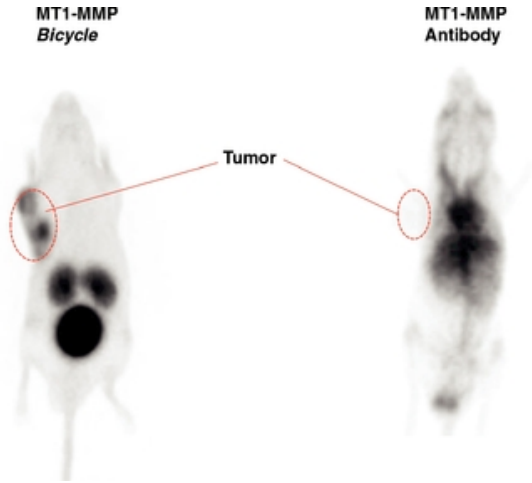
- ***Larger toxin payload.*** Despite the small size of *Bicycles*, they are able to carry a larger dose of toxin per unit mass than a comparator ADC. Therefore, we believe that *Bicycles* can deliver a higher concentration of the linked toxin to increase the probability of tumor killing.

- ***Manufacturing.*** The fully synthetic process by which *Bicycles* are manufactured facilitates ease and consistency of manufacturing and improved formulation compared to ADCs.

In order to compare the ability of a *Bicycle* conjugate and an antibody conjugate to penetrate a tumor, using positron emission tomography, or PET, imaging, we compared a radiolabeled

Bicycle to an antibody directed at the same target in a preclinical rodent study. As shown in the figure below, we observed that 15% to 20% of the injected dose per gram was detected after administration of the *Bicycle* in the tumor at 40 to 60 minutes, with no antibody detectable in the tumor during this time. We also observed accumulation of the balance of the *Bicycles* in the bladder and kidneys, indicating rapid renal excretion. In contrast, the antibody was detected in the vasculature.

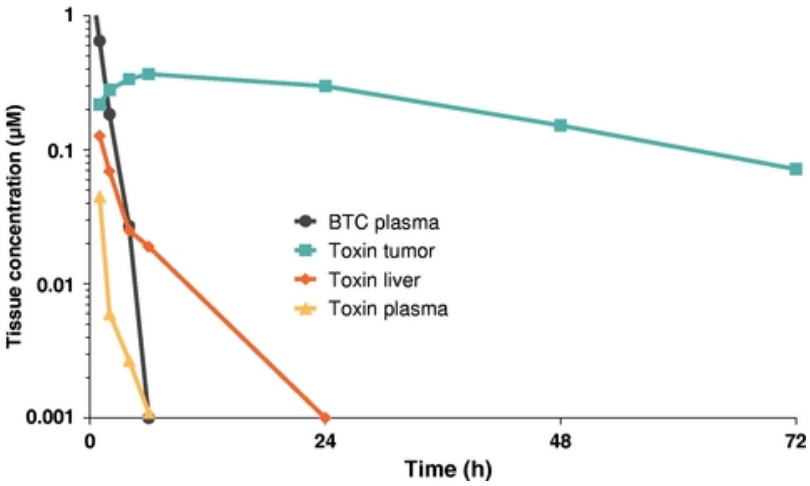
PET Imaging Revealing Payload Delivery in a Mouse Model



In addition, in a preclinical rodent study using photoacoustic imaging, we observed that *Bicycles* were retained in the tumor for 24 hours and at levels substantially in excess of those observed with a comparator antibody.

The figure below summarizes the results of a preclinical rodent xenograft model that investigated payload concentrations over time in different organ systems after administration of a BTC. In this model, we observed the toxin payload was retained in the target-expressing tumor over time, but was rapidly eliminated from other tissues.

Payload Concentrations Over Time in Different Organ Systems After Administration of a BTC

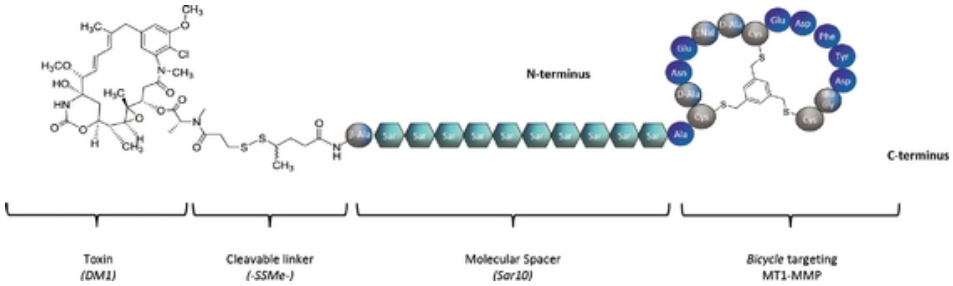


We believe these data demonstrate the potential of BTCs to have long-term sustained activity and to limit the toxicity that is associated with ADCs.

BT1718

Our lead product candidate, BT1718, is a BTC that we are developing for oncology indications. The molecule is comprised of our MT1-MMP targeting *Bicycle*, a hindered disulphide cleavable linker and a cytotoxin DM1 payload.

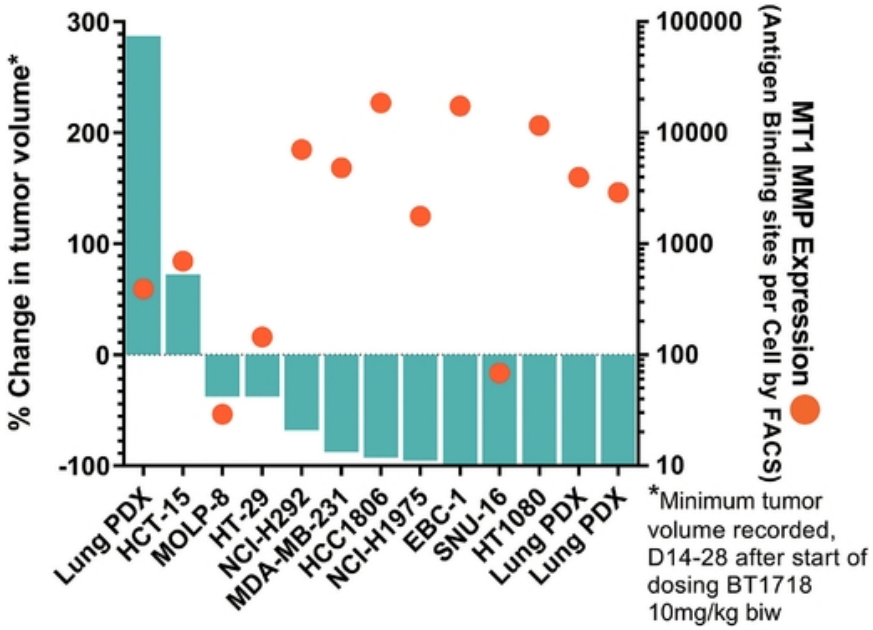
Schematic of BT1718



MT1-MMP is a matrix metalloprotease involved in tissue remodeling and is generally expressed at relatively low levels in normal adult tissues. MT1-MMP has an established role in cell invasion and metastasis, and we believe that MT1-MMP is an attractive target for cytotoxin delivery due to its high level of expression on stromal and tumor cell subsets in various cancers. We estimate that MT1-MMP expression ranges from approximately 58% to up to 100% of the ovarian, bladder, lung, endometrial and triple negative breast cancer samples we have tested, depending on cancer type.

In our preclinical studies, we observed that BT1718 was associated with the greatest anti-tumor effect when membrane expression of MT1-MMP was high (as quantified by fluorescence activated cell sorting, or FACS). Tumors with lower levels of expression of MT1-MMP were observed to have reduced levels of response to BT1718. We are collaborating with leading cancer researchers to determine MT1-MMP expression levels across a panel of tumor types, which will help inform patient selection for further clinical development. One of the goals of our clinical trials is to better understand the relationship between the level of target expression and activity of BT1718.

Effect of MT1-MMP Expression on BT1718 Activity Across Preclinical Xenograft Models



We are not aware of any other cytotoxin conjugates in development that target MT1-MMP.

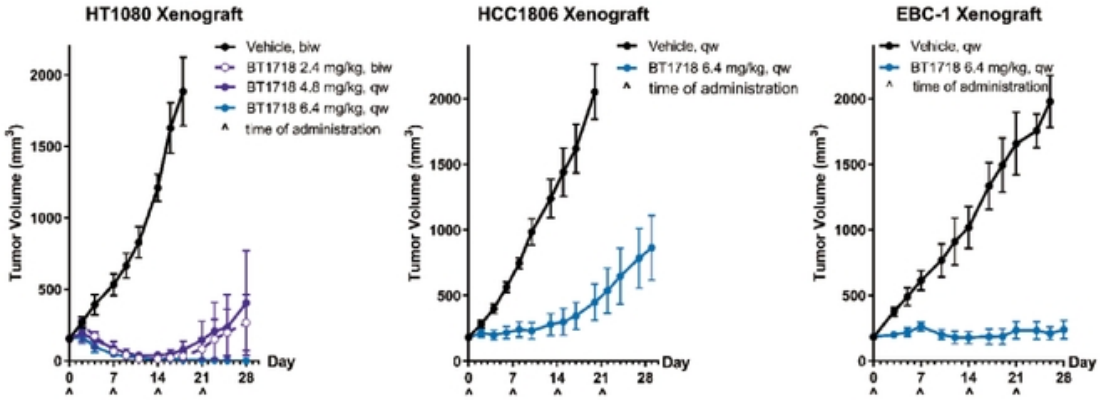
Preclinical Experience

BT1718 has been dosed in multiple species, including rodents and non-human primates. In *in vivo* preclinical studies, we observed dose-dependent anti-tumor activity following administration of BT1718 with disease stabilization or regression in multiple xenograft models across tumor types including lung, breast, gastric, head and neck, fibrosarcoma and colorectal. These models utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor and measured through the course of the preclinical study and at the end of the preclinical study to evaluate the activity of BT1718. A 3 mg/kg dose of BT1718 administered biweekly was observed to be associated with stable disease or tumor regression in several models. Further, the highest dose of BT1718 tested, 10 mg/kg administered biweekly, was observed to be associated with complete regressions in the majority of MT1-MMP-expressing xenograft tumors tested, with most mice remaining tumor-free for up to 60 days after the last dose, following which the study ended. In addition, weekly dosing of 6.4 mg/kg of BT1718 (corresponding to a 19.2 mg/m^2 human equivalent dose) was observed to be associated with significant anti-tumor activity or complete responses in a range of cell line derived xenograft models, including HT1080-, HCC1806- and EBC-1.

Mouse Dose to Human Equivalent Dose Conversion

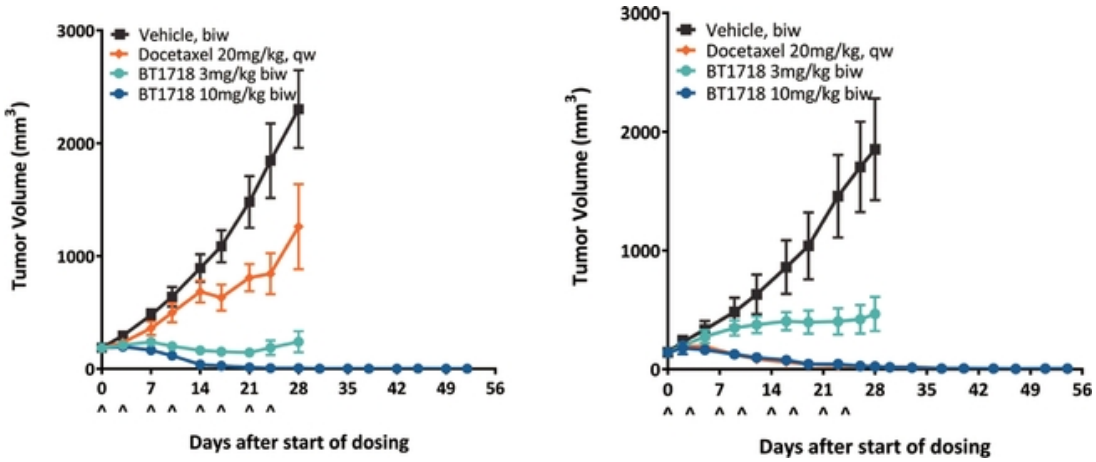
Mouse Dose (mg/kg)	Human Equivalent Dose (mg/m^2)
2.4	7.2
3.0	9.0
4.8	14.4
6.4	19.2
10.0	30.0

Effect of Administration of BT1718 in Cell Line Derived Xenograft Models



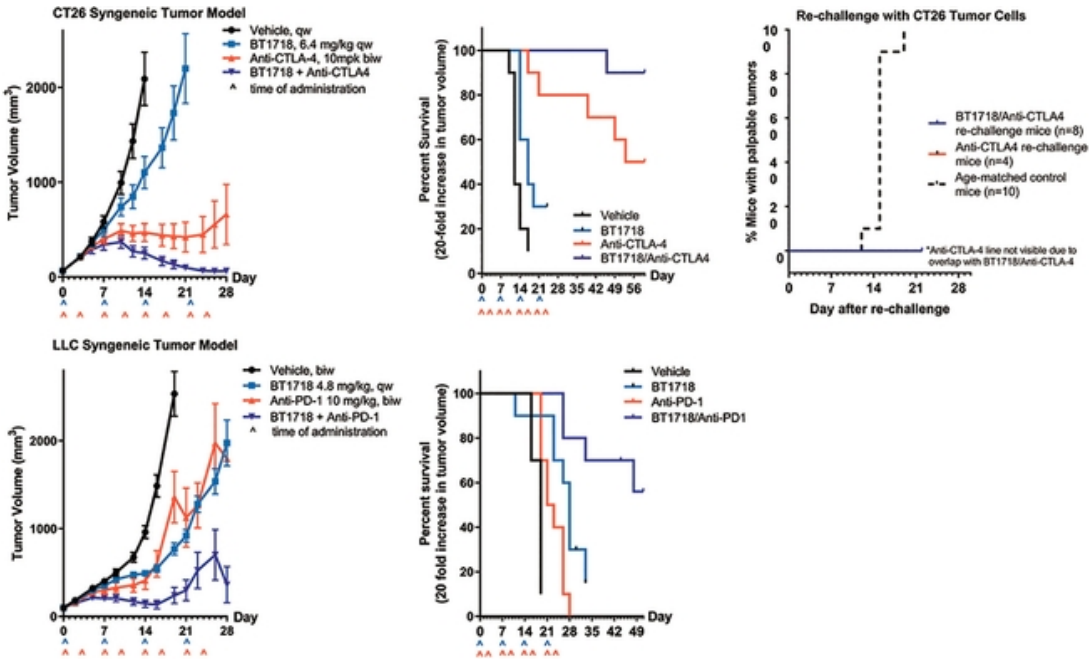
Patient-derived xenograft, or PDX, models are designed to capture patient responses to oncology therapy in a heterogeneous cohort of patients with solid tumors with 80-100% correlation between the PDX and patient response. BT1718 was also evaluated in two lung adenocarcinoma PDX models, one sensitive to, and one resistant to, docetaxel, a marketed chemotherapy medication. In both cases, we observed that BT1718 treatment at a dose of 3 mg/kg administered twice per week was associated with a significant reduction of tumor volume. Further, a 10 mg/kg dose of BT1718 administered twice per week was associated with complete and durable regression of tumors. In the docetaxel resistant model, we observed that BT1718 at both doses tested was associated with statistically significant responses, whereas docetaxel, at its maximum-tolerated dose, was not. To determine whether data is statistically significant, we use a "p-value," which represents the probability that random chance could explain the results. Generally, a p-value less than 0.05 is considered statistically significant, and may be supportive of a finding of efficacy by regulatory authorities. However, regulatory authorities, including the FDA and EMA, do not rely on strict statistical significance thresholds as criteria for marketing approval and maintain the flexibility to evaluate the overall risks and benefits of a treatment. If not otherwise specified, we used a conventional 5% or lower p-value ($p < 0.05$) to define statistical significance for the clinical trials and studies and data presented in this prospectus. These models utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor and measured through the course of the preclinical study and at the end of the preclinical study to evaluate the activity of BT1718.

Effect of BT1718 on Tumor Volume in Preclinical Patient-Derived Xenograft Models



BT1718 was also evaluated in murine syngeneic tumor models in combination with checkpoint inhibitors. BT1718 in combination with anti-cytotoxic T-lymphocyte-associated protein 4, or anti-CTLA-4, antibody was associated with significant anti-tumor activity including complete responses, enhanced survival and development of immunogenic memory in the CT26 syngeneic tumor model. Development of immunologic memory was determined as a failure to establish tumor growth after tumor cell implantation in animals that had been cured 60 days after treatment initiation with either BT1718 in combination with anti-CTLA-4 (8/10 mice) or anti-CTLA-4 monotherapy (4/10 mice). Furthermore, BT1718 in combination with anti-PD-1 antibody was associated with significant anti-tumor activity and enhanced survival in the syngeneic tumor model.

Effect of BT1718 Combination Therapy with Anti-CTLA-4 Antibody or Anti-PD-1 Antibody in Preclinical Syngeneic Mouse Tumor Models



We also evaluated the PK profile of BT1718 in several *in vivo* preclinical studies. In these studies, we observed that BT1718 exhibited a consistent PK profile across species, as well as behavior consistent with our expectations of a BTC, including a volume of distribution approximately equal to extracellular fluid, rapid clearance and a short systemic half-life. These studies utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor and measured through the course of the preclinical study and at the end of the preclinical study to evaluate the activity of BT1718.

Pharmacokinetic Profile of BT1718

Preclinical Species	Clearance (CLp; mL/min/kg)	Volume of distribution (Vss; L/kg)	Terminal half-life ($t^1/2$; hours)
Mouse	8.4	0.20	0.3
Rat	9.4	0.29	0.6
Non-Human Primate	8.0	0.20	0.4

Clinical Development

Ongoing Phase I/IIa First in Human Clinical Trial

BT1718 is being investigated in an ongoing Phase I/IIa open label dose escalation and expansion clinical trial sponsored by CRUK. Up to 40 patients with advanced solid tumors are being enrolled in the ongoing Phase I part of this trial at three sites in the United Kingdom in which two dosing regimens are being evaluated.

The Phase I part of this clinical trial is enrolling patients with advanced solid tumors, regardless of tumor MT1-MMP expression levels to evaluate the safety and tolerability of BT1718

and establish a recommended Phase 2 dose using two dosing schedules, twice per week and once per week, each as one-hour intravenous infusions. In addition, BT1718 and toxin PK profiles, preliminary efficacy, pharmacodynamic and predictive biomarkers will be explored. We expect to update preliminary data from the Phase I part of this clinical trial in the second half of 2019.

Once a recommended Phase 2 dose has been determined, the Phase IIa part of the trial is expected to commence, which we expect to occur in the second half of 2019. In this part of the trial, patients with tumors that express MT1-MMP will be enrolled and we will determine tumor types for investigation in this part of the trial in conjunction with CRUK. To determine tumor types of interest, a clinically validated MT1-MMP immunohistochemistry assay, or IHC, developed in collaboration with CRUK, was used to screen tumor tissue microarrays, or TMA, from multiple tumor types selected based on literature reports of high expression of MT1-MMP, including breast, lung, sarcoma, gastric, ovarian endometrial, bladder, and esophageal cancers. The Phase IIa part will be conducted at up to six sites in the United Kingdom. We plan to enroll patients in up to four expansion cohorts administered with our once-weekly dose. Each cohort will evaluate 16 patients with a specified tumor type determined using the results of the MT1-MMP IHC TMA analysis.

We expect the endpoints for the Phase IIa part of this clinical trial will be safety and preliminary efficacy in patients with tumors expressing MT1-MMP. Archived tumor samples from all enrolled patients will be collected and tested for MT1-MMP expression using the clinically validated IHC and associations with tumor and stromal expression and clinical response will be explored. Biopsies of tumors will be mandatory in a subset of patients in this part of the study in order to evaluate tumor PK and pharmacodynamic biomarkers of response to BT1718.

The Phase I part of the clinical trial commenced in early 2018 and this part of the trial remains ongoing. As of May 9, 2019, nine cohorts of patients (N = 24) have been dosed and evaluated with doses ranging from 0.6 mg/m^2 to 20 mg/m^2 on either a once weekly or twice weekly dosing schedule. Based on data received and to align with a more patient-centric strategy, we decided to focus investigation on a once-weekly dosing schedule. For the once a week schedule, two cohorts have been completed at doses of 9.6 mg/m^2 and 15 mg/m^2. In these cohorts, BT1718 exhibited a sufficiently favorable tolerability profile to enable dose escalation such that patients are currently being enrolled into a 20 mg/m^2 dose cohort. We observed that following two cycles of the once-weekly dose 9.6 mg/m^2 administered in cycles every three of four weeks, all of the three patients in the cohort had stable disease at first disease evaluation. As of May 9, 2019, one patient continues to have stable disease following six cycles of treatment and two patients have exited the study due to disease progression. We observed that following two cycles of the once-weekly dose of 15 mg/m^2 administered in cycles every three of four weeks, two out of three patients had stable disease at first disease evaluation. As of May 9, 2019, one of three patients in this cohort remains on study with stable disease following four cycles of treatment and two patients have exited the study due to disease progression. Two of three patients in the once weekly 20mg/m^2 cohort administered in cycles every three of four weeks were determined to have stable disease at the time of first assessment. As of May 9, 2019, one patient in this cohort remains on study, one patient exited the study due to disease progression and the other patient is not yet evaluable. Across the once- and twice-weekly cohorts, tolerability was generally favorable. Two dose-limiting toxicity events were recorded in the twice weekly cohort: a Gamma-Glutamyl Transferase, or GGT, elevation was observed in a patient with prior history of repeated GGT elevation and a grade three fatigue was observed in the second patient. The recommended dose for the weekly schedule is expected to be established in the second half of 2019.

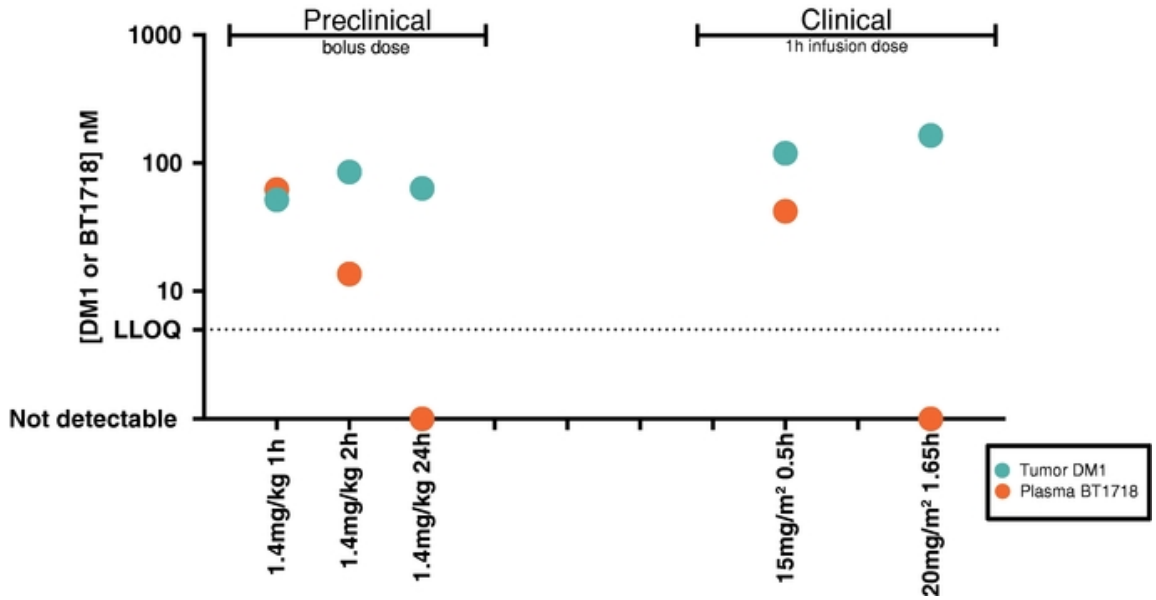
Based on the data available to date, the pharmacokinetics of BT1718 are linear with dose, with BT1718 exhibiting a moderate plasma clearance (CLp; approximately 10 mL/min/kg) with a volume of distribution similar to extracellular fluid (Vss; approximately 0.20 L/kg) and a resultant plasma

terminal half-life of approximately 0.3 hours. Based on this preliminary clinical pharmacokinetic data, we believe that the clinical pharmacokinetic profile of BT1718 is consistent with preclinical data.

BT1718 is designed to deliver relatively larger payloads of DM1 compared to other drug conjugate approaches. For example, Kadcyla is a marketed ADC from Genentech containing a HER2-targeted antibody and DM1. The maximum recommended clinical dose of Kadcyla is 3.6 mg/kg every three weeks, equivalent to a dose level of 2.45 mg/m^2 of DM1. BT1718 is administered weekly for three weeks followed by a one week suspension. The current weekly dose BT1718 is 20 mg/m^2, equivalent to a dose level of 4.20 mg/m^2 of DM1. Over an equivalent dosing cycle of 12 weeks, BT1718 can deliver a total DM1 payload of 37.80 mg/m^2 of DM1 compared to only 9.80 mg.m^2 with Kadcyla. BT1718 has the potential to deliver up to four fold more DM1 than Kadcyla at that dose level.

Based on an analysis of clinical tumor biopsy samples, tumor targeting and retention of the DM1 cytotoxin payload in patients has been exhibited. Concentrations of DM1 in clinical tumor biopsy samples are consistent with preclinical data obtained at doses that gave partial (4.2 mg/m^2) and full (14.4 mg/m^2) tumor regression doses in mouse xenograft models.

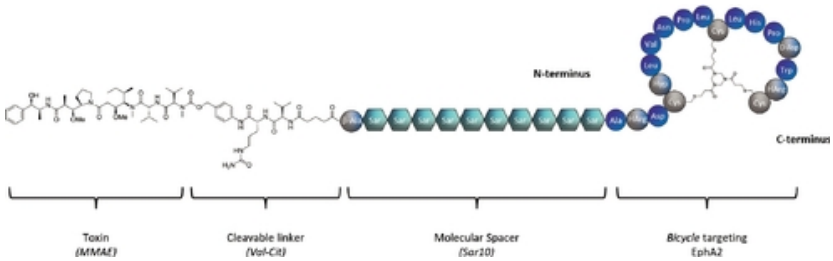
DM1 Levels in Clinical and Preclinical Tumor Samples



BT5528

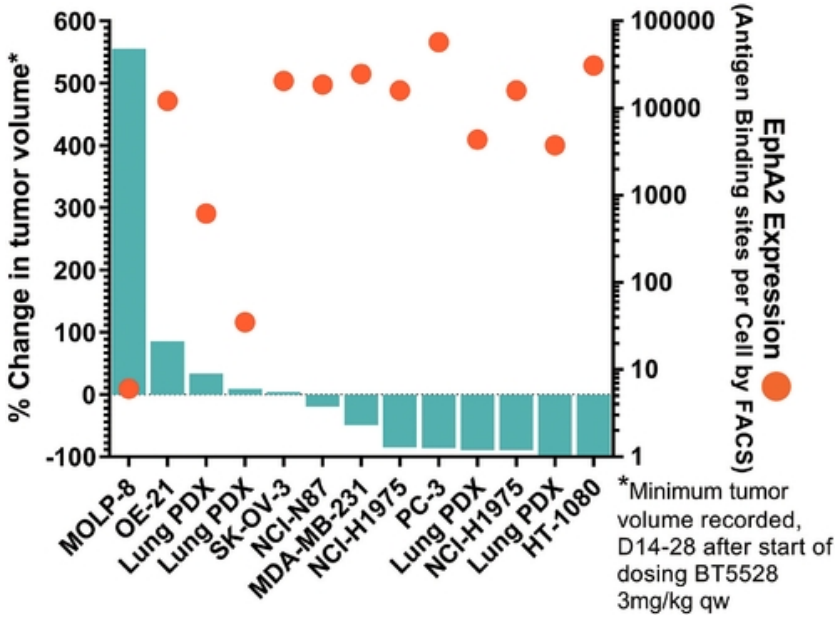
BT5528 is a BTC designed to target EphA2. The molecule is comprised of our EphA2 targeting *Bicycle*, a valine-citrulline, or val-cit, cleavable linker and a cytotoxin MMAE payload.

Schematic of BT5528



EphA2 is a member of the Ephrin superfamily of receptor tyrosine kinases regulating cell migration, adhesion, proliferation and differentiation. EphA2 is expressed at relatively low levels in normal adult tissues, but is overexpressed in numerous difficult to treat tumors including lung, breast, bladder, gastric, ovarian, endometrial, cervical, melanoma, esophageal, pancreatic, and glioma. In both cell-derived and patient-derived preclinical models, we observed anti-tumor activity signals following administration of our EphA2 toxin conjugates, which correlated with EphA2 expression, as determined by FACS studies.

Effect of EphA2 Expression on BT5528 Activity Across Preclinical Xenograft Models



EphA2 has previously been pursued by other companies utilizing ADCs. However, significant safety concerns, including bleeding events and liver toxicity, were observed in preclinical studies and early clinical development, which resulted in the discontinuation of development. For example, in a Phase I clinical trial of MEDI-547, an EphA2 targeting ADC, an increase in the liver enzyme ALT and AST was observed in half of the dosed patients and bleeding events were observed in five out of six patients, in each case within two to eight days following a single dose. The bleeding events observed in humans from the clinical trial were consistent with findings from the preclinical studies in other species, including primates.

We believe EphA2 is an attractive target for our BTCs due to the potential of *Bicycles* to overcome the safety concerns observed with ADCs. In our preclinical PK and toxicokinetic studies, we observed a short half-life and volume of distribution similar to BT1718. We observed that the accumulation of MMAE in the tumor tissue led to mitotic arrest of tumor cells and tumor regression was evident within days of administration. Due to the shorter half-life, improved penetration into solid tumors and kidney elimination, we believe that BT5528 could address the challenges of ADCs. Similar to the strategy for selecting indications for BT1718, we plan to screen tumor TMAs using a clinically validated EphA2 IHC, in a CAP accredited and CLIA certified laboratory, to prioritize those indications with high EphA2 protein expression for clinical investigation.

Our IND-enabling preclinical studies for BT5528 are currently ongoing.

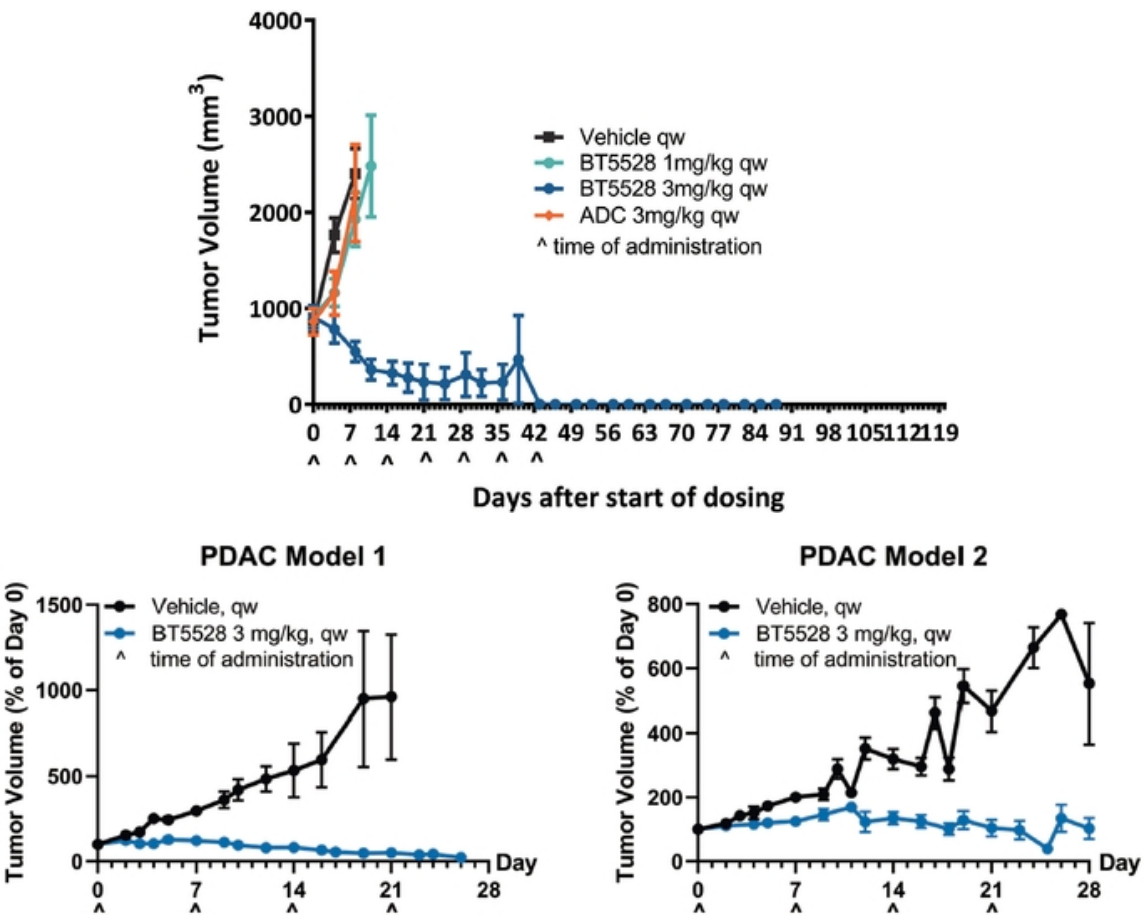
Preclinical Experience

BT5528 has been evaluated in preclinical studies in multiple species, including rodents and non-human primates. In our preclinical studies, BT5528 was not observed to have a significant effect on clotting parameters and did not exhibit abnormal liver function at tolerated doses. We also observed no bleeding events in primates at toxin equivalent doses over 150-fold higher than the clinical dose of an ADC with the same amino acid sequence and with the same linker-toxin combination and average drug/antibody ratio as MEDI-547 used in patients. These studies utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor, measured through course of experiment and at experiment end to evaluate the activity of BT5528.

In *in vivo* preclinical studies, we observed dose-dependent anti-tumor activity following administration of BT5528 with disease stabilization or regression in multiple xenograft models representing tumor types including lung, breast, gastric, fibrosarcoma, prostate, ovarian and oesophageal, with activity correlating with EphA2 expression. We observed that a dose of 1 mg/kg of BT5528 administered weekly was associated with stable disease or tumor regression in several models. Complete regressions were observed in the majority of EphA2-expressing xenograft tumors in mice administered 2 mg/kg or 3 mg/kg of BT5528 weekly, with most mice remaining tumor-free for more than 60 days after dose cessation, following which the study was ended. These studies utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor and measured through the course of the preclinical study and at the end of the preclinical study to evaluate the activity of BT5528. In separate pharmacokinetic studies, the concentration of MMAE toxin was determined in the tumor and plasma following a single intravenous administration of 0.5 mg/kg of BT5528, indicating the efficient delivery of MMAE to the tumor by BT5528.

As shown in the figure below, we observed that BT5528 displayed superior activity to an EphA2 targeting ADC in a mouse PDX model. In this model, the tumors were large (approximately 1,000 mm^3) at the commencement of dosing. The tumor was derived from a docetaxel resistant non-small cell lung cancer from a 74 year-old male smoker with moderate EphA2 expression. BT5528 was dosed once weekly. BT5528 was also evaluated in two pancreatic ductal adenocarcinoma (PDAC) PDX models. BT5528 treatment at a weekly dose of 3 mg/kg was associated with a significant reduction of tumor volume. We also compared the distribution of an EphA2 BTC and an EphA2 ADC using PET imaging in a preclinical rodent study. The *Bicycle* was detected in the tumor at 60 minutes, as well as in the bladder and kidneys. In contrast, the antibody was not detected in the tumor at 60 minutes but was restricted to the vasculature.

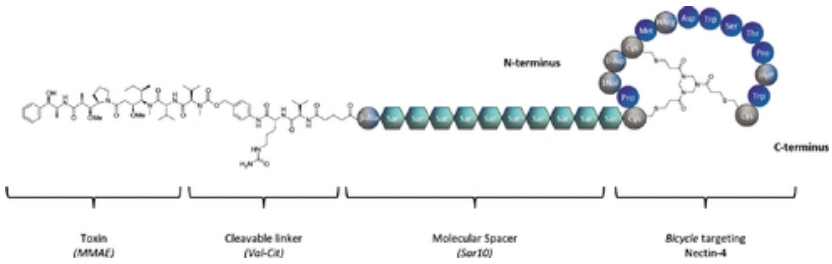
Effect of BT5528 on Tumor Volume in Preclinical Patient-Derived Xenograft Models



BT8009

BT8009 is a BTC designed to target Nectin-4. The molecule is comprised of our Nectin-4 targeting *Bicycle*, a val-cit cleavable linker, and a cytotoxin MMAE payload.

Schematic of BT8009

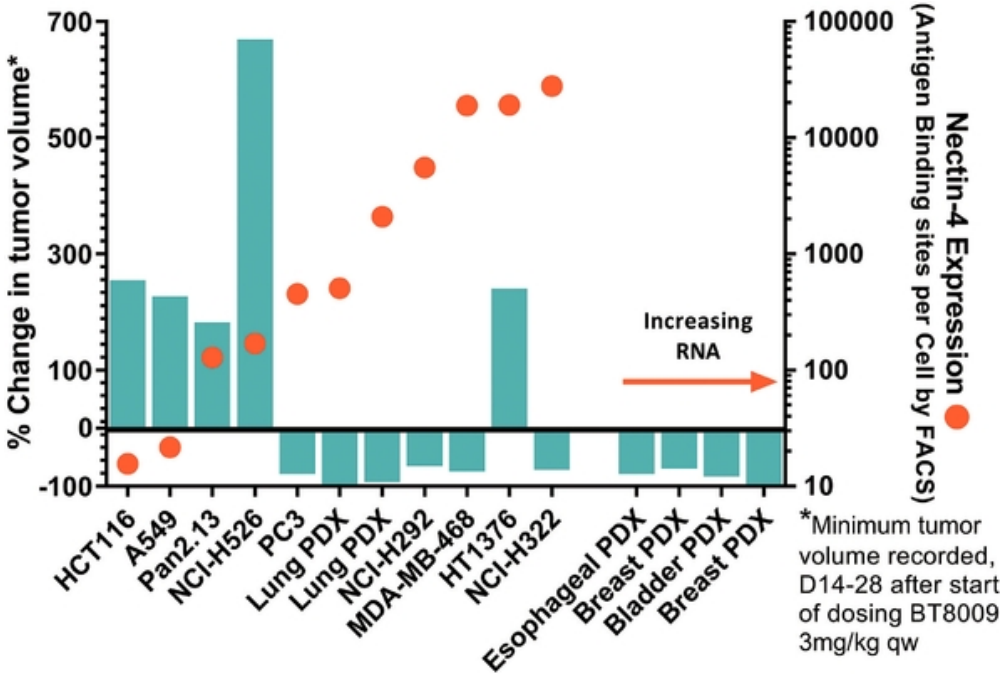


Nectin-4 (also known as PVRL4) is a cell adhesion molecule from the Nectin and Nectin-like family, members of which are integral to the formation of the homotypic and heterotypic cell

junctions. Nectin-4 has been shown to be overexpressed in tumor cells and is believed to play a role in tumor cell growth and proliferation. High in normal embryonic and fetal tissue, Nectin-4 declines in adulthood, showing a limited distribution in healthy tissues. However, Nectin-4 is expressed on tumor cells in numerous cancer types including bladder, breast, gastric, lung and ovarian. In addition, we believe the favorable characteristics of BTC-targeted therapies may address some of the challenges in treating pancreatic cancer.

We have observed that BT8009 efficiently delivered MMAE to the tumor and had a broad spectrum of activity that correlated with Nectin-4 expression, as determined by FACS studies or RNA levels.

Effect of Nectin-4 Expression on BT8009 Activity Across Preclinical Xenograft Models



We are aware of one Nectin-4 ADC program in development, which is being jointly conducted by Seattle Genetics and Astellas, and is currently in Phase III clinical development. Similar to the strategy for selecting indications for BT1718 and BT5528, we plan to screen tumor TMAs using a clinically validated Nectin-4 IHC to prioritize indications with high Nectin-4 protein expression for clinical investigation.

Our IND-enabling preclinical studies for BT8009 are currently ongoing.

Preclinical Experience

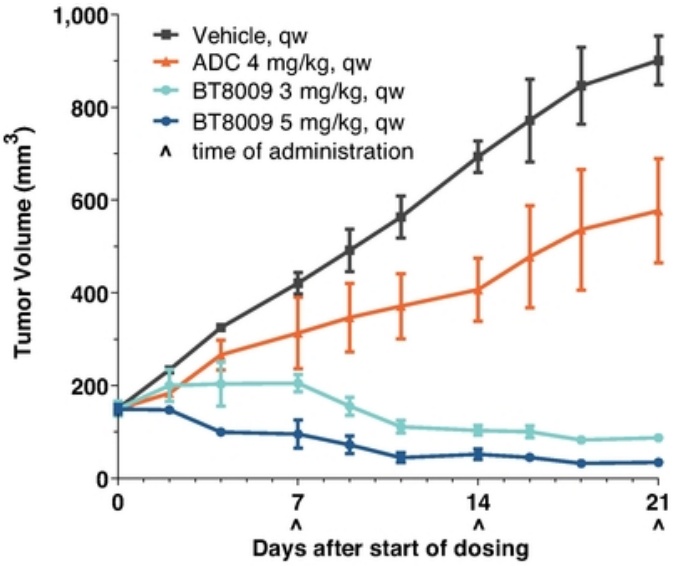
In *in vivo* preclinical studies, we observed that BT8009 was associated with dose-dependent anti-tumor activity with disease stabilization or regression in multiple xenograft models representing tumor types including lung, breast, and esophageal cancers. We observed that BT8009 activity was correlated with either Nectin-4 protein or mRNA expression. We observed that a dose of 3 mg/kg of BT8009 administered weekly was associated with complete regression in multiple models. We also observed complete regression of large (1,000 mm^3 starting volume) MDA-MB-468 breast cancer tumors at a dose of 5mg/kg given every 14 days. In two models, there was no observed tumor

regrowth at 59 days after the last administration, following which the study was ended. These studies utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor and measured through the course of the preclinical study and at the end of the preclinical study to evaluate the activity of BT8009.

In head to head preclinical studies comparing BT8009 to an ADC with the same amino acid sequence and with the same linker-toxin combination and average drug/antibody ratio as enfortumab vedotin displayed comparable or superior activity to the ADC in three cell-derived xenograft studies and five PDX models. These studies utilized an endpoint of tumor volume, as calculated from standard caliper measurements of subcutaneous tumor and measured through the course of the preclinical study and at the end of the preclinical study to evaluate the activity of BT8009.

The figure below illustrates results from a preclinical non-small cell lung cancer cell-derived xenograft. In that model, we observed that BT8009 showed a superior activity at early timepoints compared to high dose administration of an ADC with the same amino acid sequence and with the same linker-toxin combination and average drug/antibody ratio as enfortumab vedotin. We also observed that administration of BT8009 was associated with complete regression of the tumor. In other models we have observed superior activity of BT8009 over docetaxel and doxorubicin as measured by decrease in tumor volume.

Effect of BT8009 on Tumor Volume in a Preclinical Non-Small Cell Lung Cancer-Derived Xenograft Model



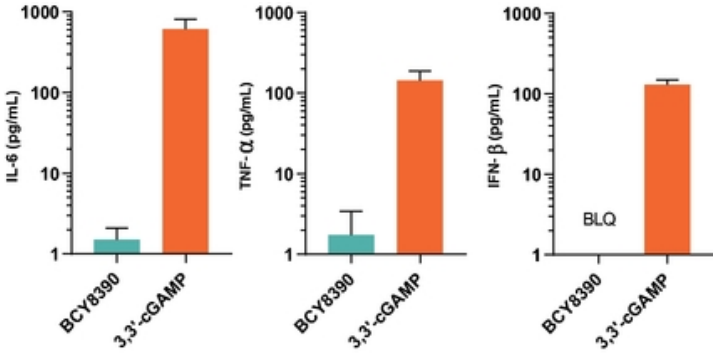
Bicycle Targeted Innate Immune Activators

Local activation of the innate immune system within tumors is a promising area for cancer drug discovery. Many of the current clinical programs require direct injection of molecules activating the innate immune system into tumors to avoid excessive systemic activation of the immune system and associated toxicity. Based on our experience with BTCs, we believe that *Bicycles* can systemically deliver activators of the innate immune system to tumors without activating the immune system in normal tissues. We believe that this approach has the potential to avoid the need for

direct tumor injection and to allow inaccessible tumors to be reached, while enabling rapid systemic elimination of excess payloads in an inactive form.

We are currently advancing this approach through the development of systemically-delivered *Bicycle* STING agonists, targeted to both novel and validated tumor targets. As shown in the figure below, in a preclinical study, a *Bicycle* conjugated to a cyclic dinucleotide STING agonist (BCY8390) delivered systemically in mice was observed to result in significantly lower serum inflammatory cytokine release, as measured by levels of IL-6, TNF-a and IFN-b (below limit of quantitation for BCY8390) as compared to the unconjugated STING agonist (3,3'-cGAMP). We believe these results support the potential for *Bicycle* innate immune activators to be systemically administered.

Effect of a Bicycle/STING Conjugate on Cytokine Release in Serum after IV Dose



Bicycle T-Cell Modulators

We are developing cytotoxic T-cell activators, designed to trigger an immune response to tumors. We have identified potent *Bicycle* activators of CD137, a tumor necrosis factor receptor, or TNFR, family member and we believe we are currently the only company that has fully chemically synthetic CD137 agonists. We believe that *Bicycles* represent a differentiated approach to target CD137 that may confer several advantages over existing modalities due to the multivalency and PK characteristics of *Bicycles*. Our *Bicycle* T-cell modulators are designed to circumvent the limitations of antibody and biologic therapies, such as liver toxicity and limited efficacy, and to better enable combination therapy.

We are also exploring CD137 in a bi-specific format linked to *Bicycles* that bind tumor antigens, inhibit checkpoint proteins or otherwise activate the immune system. We believe we are currently the only company that has fully chemically synthetic bi-specific CD137 agonists.

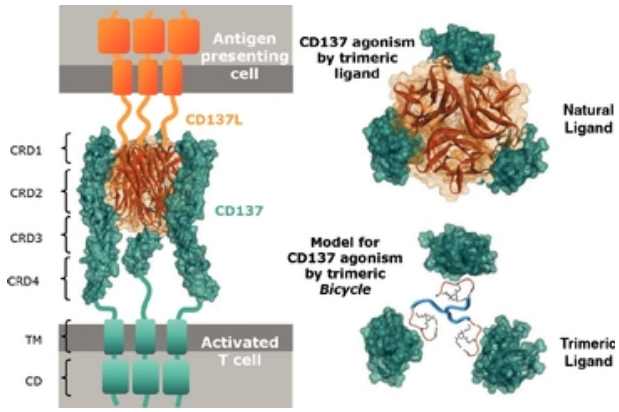
Approaches that activate cytotoxic T-cells, a type of cell used in a body's immune response, have been observed to improve outcomes in cancer. However, prolonged immune activation can be toxic and lead to T-cell exhaustion, which is a challenge amplified by the long half-life of antibodies and biologics that are often used in these treatment approaches. We believe the differentiated properties of *Bicycles* may allow us to develop molecules with a pharmacodynamically distinct and improved profile over existing therapies.

We are aware of anti-CD137 antibodies undergoing clinical testing, including urelumab being developed by Bristol-Myers Squibb, which produced single agent responses but also severe liver toxicity, and utomilumab being developed by Pfizer, which exhibited minimal clinical activity with less toxicity.

Properties of Bicycle T-Cell Modulators

In order to activate the CD137 receptor, cross-linking of a trimeric receptor is required. As a result, we are developing trimeric and tetrameric molecules that cross-link the receptor into an active form as shown in the image below.

Schematic of a Proposed Trimeric CD137 Bicycle Agonist



These *Bicycle* multimers feature the following favorable pharmacological characteristics for immuno-oncology therapeutics. We believe these characteristics have the potential to overcome the limitations of antibodies and fusion proteins.

- ***Simplicity and small size.*** Our trimeric and tetrameric *Bicycles* are chemically synthesized and are very small in comparison to other molecules targeting the CD137 receptor. For example, the approximate molecular weight of urelumab is 146 kDa. In contrast, the molecular weight of our tri-and tetrameric *Bicycles* are in the range of approximately 9 kDa to 15 kDa, which is designed to facilitate the rapid penetration of the therapeutic into tumor tissue.

- ***Tunable PK.*** *Bicycles* are amenable to chemical modifications that allow the PK of the multimers to be fine-tuned. We believe this enables the development of molecules with the optimal balance of prolonged CD137 agonism, but with rapid enough elimination from systemic circulation to avoid the undesired toxicities of CD137, as has been observed with urelumab. In addition, this tunable half-life is expected to enable different sequences of therapeutics to be evaluated in the clinic potentially reducing the risk of overlapping toxicities.

- ***Renal elimination.*** Rapid renal elimination may avoid liver toxicity observed with other CD137 agonists in development.

- ***Modular.*** The modular nature of *Bicycles* permits the presentation of CD137 binders in various orientations allowing us to design molecules with a range of activities. We believe that we can select the optimal activity profile to avoid the weak efficacy seen with the utomilumab molecule or the overstimulation of CD137 by urelumab that resulted in systemic toxicity.

Comparison of the Features of our Bicycle T-Cell Modulators to Biological T-Cell Modulators

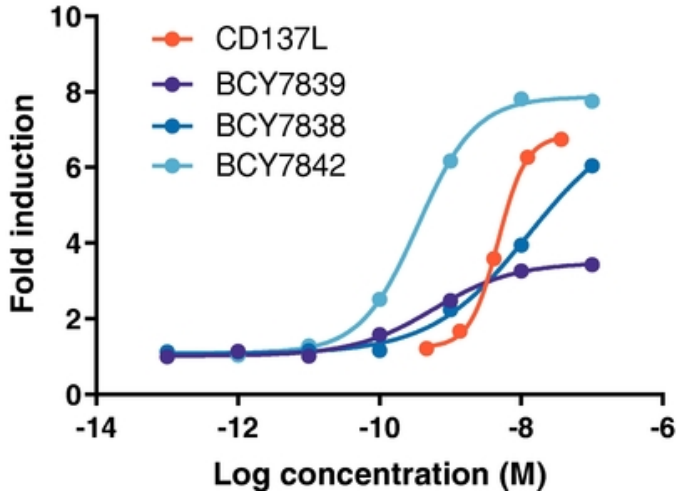
Limitations of multivalent and bi-specific biologics	*Bicycles* potentially overcome these limitations
Pharmacology	
• Very large molecules: (~150-350 kDa) for multimeric; ~40-200 kDa for bi-specific • Limits on presentation of binding domain to the target results in fixed orientation • Difficult to make a molecule bind to more than two targets • High chance for immunogenicity as the size and complexity increase	• Very small: (~9-15 kDa) for multimeric; ~3.5-5 kDa for bi-specific • Linkage through various sites of attachment allows presentation of binder in various orientations • Easy to make tri- and tetrameric molecules • Immunogenicity unlikely—multimeric molecules are still smaller than smallest monovalent antibody
Manufacturing	

• Low yield (even for research scale ~10 mg)
  • Requires another optimization of the molecule even if the parent molecules are fully optimized
• Increase in heterogeneity
  • Requires more controls and stringent potency assays
	• Simple chemical synthesis
	• Chemically defined, new chemical entity

Preclinical Experience

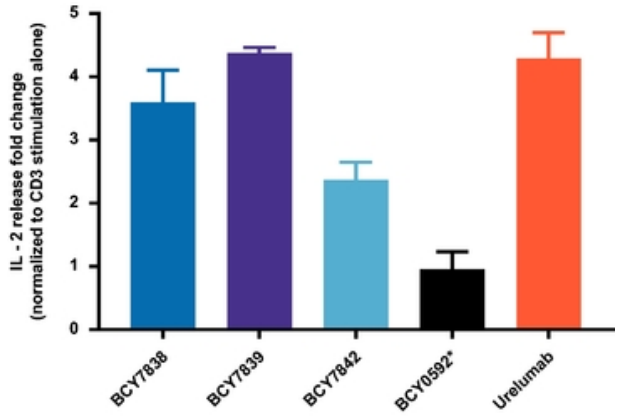
We observed that simple multivalent *Bicycle* CD137 agonists (BCY7839, BCY7838 and BCY7842) displayed potent activity in preclinical cell-based assays. As shown in the figure below, several *Bicycle* CD137 agonists displayed comparable or higher fold induction compared to the natural ligand (CD137L) in an engineered reporter cell assay whereby CD137 activation leads to production of a luminescence signal. In the figures below, fold induction refers to the ratio of luminescence signal in the cells treated with CD137 agonists compared to untreated cells.

Activity of Bicycle CD137 Agonists Compared to the Natural Ligand



As shown in the figure below, we also observed *Bicycles* stimulated the release of the cytokine IL-2, a marker of immune response, from primary human T-cells to a comparable degree as urelumab, which we believe provides meaningful evidence of activity.

Effect of CD137 Bicycles on Immune Response



* Negative control non-agonist *Bicycle*

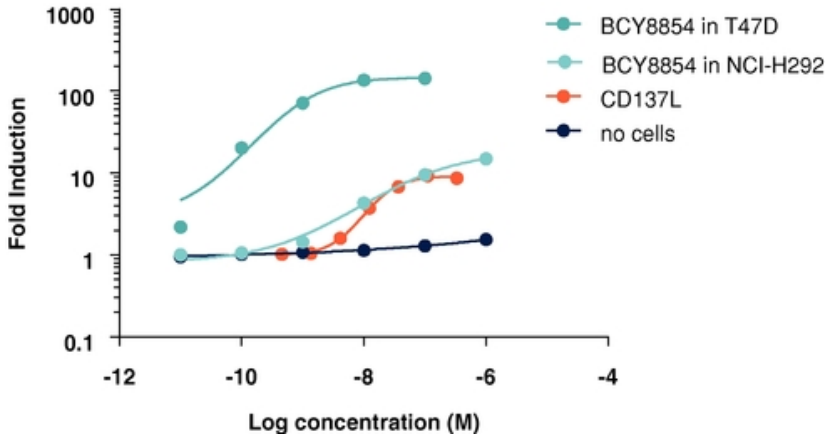
In additional *in vivo* studies, we observed that CD137 *Bicycles* increased the cytotoxic T-cell infiltration in tumor tissue. The *Bicycles* did not significantly change the expression of CD137 on tumoral T-cells while urelumab led to a decrease in the target cell population. We believe this increased cytotoxic T-cell infiltration correlates with the anti-tumor activity of the *Bicycle* CD137 agonists.

Bi-Specific Approach

In preclinical studies, we have also linked CD137 binding *Bicycles* to tumor antigen targeting *Bicycles*. We constructed multiple bi-specific molecules and observed that these bi-specific molecules agonize the CD137 receptor only in the presence of cells that express the appropriate tumor antigen.

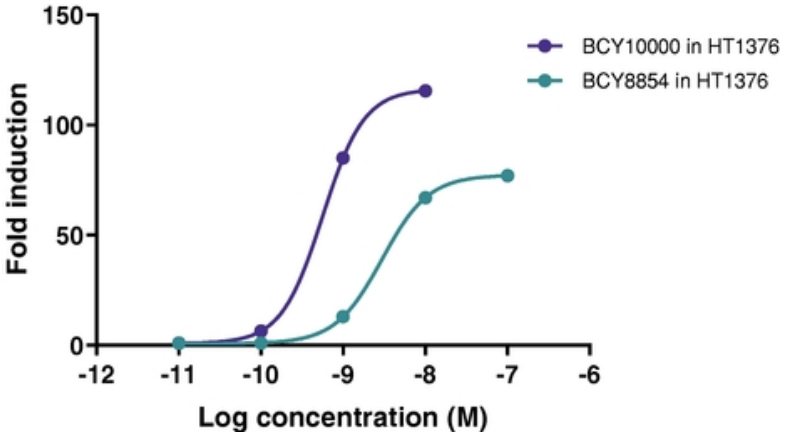
As shown in the figure below, we observed that a bi-specific Nectin-4-CD137 agonist (BCY8854) demonstrated agonist activity in a CD137 reporter assay only when tumor cells expressing Nectin-4 were present, with the degree of induction dependent on the level of Nectin-4 expression. With a high expressing cell line (T47D), the activation of CD137 by the bi-specific molecule was observed to be significantly higher than the natural ligand (CD137L) and when a low expressing cell line (NCI-H292) was tested, activation was lower.

Activity of Bi-specific CD137 Bicycle Agonist



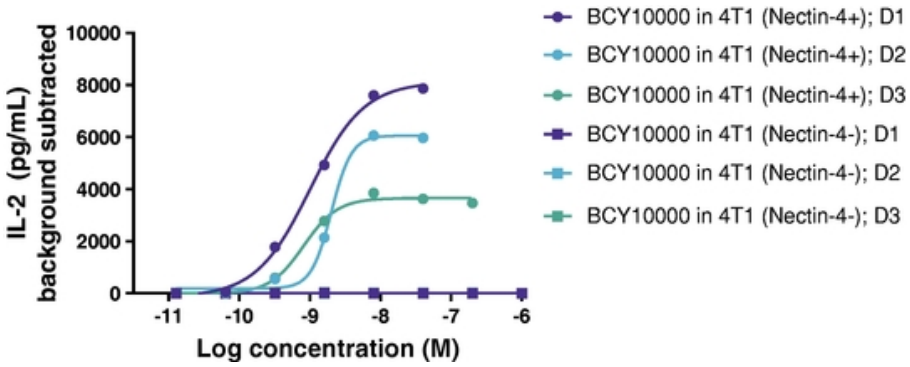
In our preclinical development of Nectin-4-CD137 bi-specific molecules, we have observed an ability to tune bi-specific molecules based on simple chemical changes, which we believe is an inherent advantage of our *Bicycle* platform-based approach to bi-specifics compared to other modalities. As an example of this, activity of two different Nectin-4-CD137 bi-specific molecules is shown below. BCY10000 was observed to have a higher affinity CD137 binding *Bicycle* than BCY8854, yielding increased activity and potency in a CD137 assay.

Tunable Activity of Bi-specific CD137 Bicycle Agonists



As shown it the figure below, we also observed that BCY10000 stimulated the release of the cytokine IL-2 from human peripheral blood mononuclear cells (PBMCS) from three independent donors (D1-D3) when in co-culture with 4T1 cells that were engineered to express Nectin-4. In co-culture with 4T1 cells lacking Nectin-4 expression, no IL-2 was produced. Data from these donors is overlapping in the figure below.

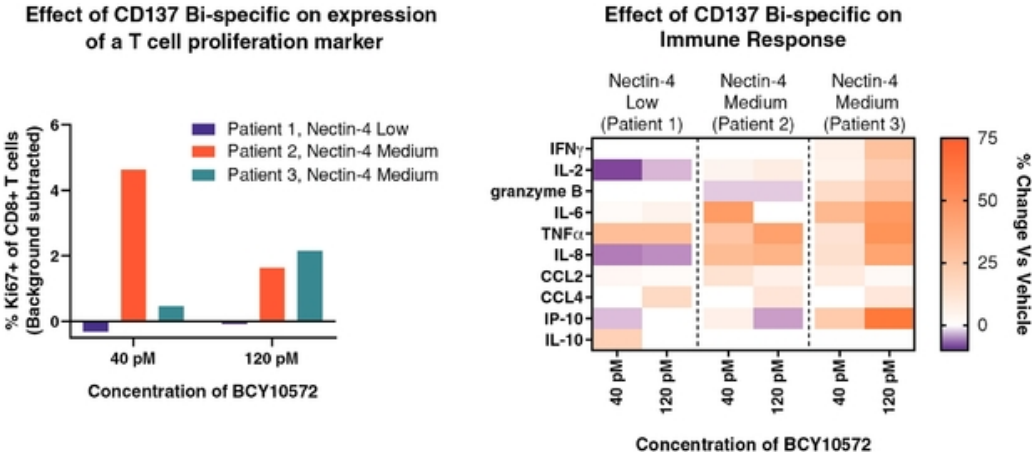
Effect of CD137 Bi-Specific on Immune Response



In additional studies, we observed that bi-specific Nectin-4-CD137 agonists at two concentrations increased the proliferation of T cells and stimulated the release of the cytokine IL-2 and other immune markers in cultures from patient-derived tumors harboring Nectin-4 expression.

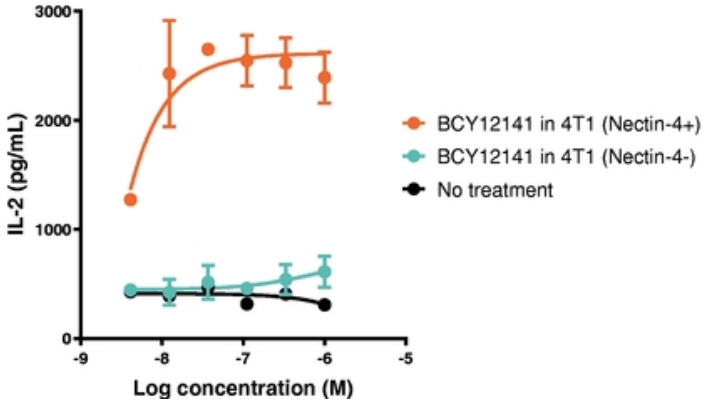
CD137 and Nectin-4 Expression in Patient Samples

	CD137+ T cells (%)	Nectin-4+ cells (%)
Patient 1	19.8	4.4
Patient 2	15.1	25.8
Patient 3	30.0	15.1



Another member of the TNF family of T-cell costimulatory receptors is TNFRSF4, also known as OX40. Using our phage platform, we discovered a *Bicycle* that binds to human OX40. A bi-specific molecule (BCY12141) combining our Nectin-4 binding *Bicycle* and OX40 binding *Bicycle* stimulated the release of the cytokine IL-2 from human PBMCs when in co-culture with 4T1 cells that were engineered to express Nectin-4. In co-culture with 4T1 cells lacking Nectin-4 expression, there was no activity observed. This is an example of how both the immune cell binding and tumor cell binding *Bicycles* can be readily interchanged in the context of our synthetic bi-specific molecules to generate novel immune agonists for further study.

Effect of OX40 Bi-Specific on Immune Response



We believe that our ability to rapidly generate and test bi-specific molecules and their simple molecular format may form the basis of additional programs in the future. In addition to the immune cell and tumor targets that we have already investigated, we are also planning to screen for, or have started to screen for, *Bicycles* that target the NK cell receptors FcgRIIIA and NKp46 as well as additional immune cell and tumor specific antigens.

Beyond Oncology

We have entered into several collaborations outside of our internal focus in oncology to leverage the broad applicability of *Bicycles*. Our strategic collaborations are based on the ability of *Bicycles* to address a wide variety of targets and we are working with collaborators with deep therapeutic expertise outside of oncology to enable us to more efficiently develop novel medicines for patients.

AstraZeneca. In November 2016, we entered into a research collaboration agreement with AstraZeneca AB, or AstraZeneca, with a focus on targets within respiratory, cardiovascular and metabolic disease.

Bioverativ. In August 2017, we entered into a collaboration agreement with Bioverativ, Inc., or Bioverativ, in the field of non-malignant hematology, including hemophilia.

Oxurion. In August 2013, we entered into a research collaboration and license agreement with Oxurion NV (formerly ThromboGenics NV), or Oxurion, focused on ophthalmology. The lead molecule of the partnership is THR-149, a novel plasma kallikrein inhibitor, for the treatment of diabetic macular edema. A Phase I clinical trial of THR-149 is currently ongoing. The Phase I clinical trial, which is being conducted by Oxurion, is an open-label, multi-center, dose escalation trial to evaluate the safety of a single intravitreal injection of THR-149 of three dose levels for the treatment of diabetic macular edema, or DME, with a primary endpoint of dose-limiting toxicities up to the Day 14 visit. On April 24, 2019, we and Oxurion announced that enrollment in the trial had been completed, with 15 patients enrolled.

Our Collaborations

Cancer Research UK

In December 2016, we entered into a clinical trial and license agreement with the Cancer Research Technology Limited and CRUK. Pursuant to the agreement, as amended in March 2017

and June 2018, CRUK's Centre for Drug Development will sponsor and fund a Phase I/IIa clinical trial of our lead product candidate, BT1718, in patients with advanced solid tumors.

CRUK is responsible for designing, preparing, carrying out and sponsoring the clinical trial at its cost. We are responsible for supplying agreed quantities of GMP materials for the study, the supply of which has been completed. In the event that additional quantities are needed, we will provide CRUK with all reasonable assistance to complete the arrangements necessary for the generation and supply of such additional GMP materials but CRUK will be responsible for supplying and paying for such additional quantities of GMP materials.

We granted to CRUK a license to our intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial. We retain the right to continue the development of BT1718 during the clinical trial. Upon the completion of the Phase I/IIa clinical study, we have the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and we decide to abandon development of all products that deliver cytotoxic payloads to the MT1 target antigen, we will assign or grant to Cancer Research Technology Limited an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case we will receive tiered royalties of 70% to 90% of the net revenue depending on the stage of development when the license is granted) less certain costs, as defined by the agreement. The CRUK agreement contains additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash and shares, with an aggregate total value of $50.9 million, as well as royalty payments based on a single digit percentage on net sales of products developed.

The CRUK agreement can be terminated by either party upon an insolvency event, material breach of the terms of the contract, or upon a change in control (and the new controlling entity generates its revenue from the sale of tobacco products). CRUK may terminate the arrangement for safety reasons or if it determines that the objectives of the clinical trial will not be met, in which case, if the study is terminated by CRUK prior to the completion of the Phase Ia dose escalation part of the study for such reasons or if CRUK refuses release of any additional quantities of GMP materials or if the parties cannot agree upon a plan to supply the additional quantities of GMP materials, we will be obligated to refund 50% of the costs and expenses incurred or committed by CRUK to perform the clinical trial. If the study is terminated by CRUK for an insolvency event, a material breach by us, or if we are acquired by an entity that generates its revenue from the sale of tobacco products, we will reimburse CRUK in full for all costs paid or committed in connection with the clinical trial and no further license payments, where applicable, shall be due. In such case where we are acquired by an entity that generates its revenue from the sale of tobacco products, CRUK will not be obliged to grant a license to us in respect of the results of the clinical trial and we will assign or grant to Cancer Research Technology Limited an exclusive license to develop and commercialize the product without Cancer Research Technology Limited being required to make any payment to us.

Non-Oncology Collaborators

Dementia Discovery Fund

In May 2019, we entered into a collaboration with the Dementia Discovery Fund, or DDF, to use *Bicycle* technology for the discovery and development of novel therapeutics for dementia. Under the terms of the agreement, Bicycle and DDF will collaborate to identify *Bicycles* that bind to clinically validated dementia targets. If promising lead compounds are identified, DDF and Bicycle will establish a jointly-owned new company to advance the compounds through further development towards commercialization. The jointly-owned company will receive a royalty and

milestone-bearing assignment and license of intellectual property from Bicycle for this purpose. DDF is a specialized venture capital fund focused on discovering and developing novel therapies for dementia.

Bioverativ

In August 2017, we entered into a research collaboration agreement with Bioverativ Inc. (acquired by Sanofi), or Bioverativ, in the field of non-malignant hematology. The Bioverativ collaboration agreement targeted two disease areas, with an option to add a third. We use our Bicycle screening platform to perform research and development services for the programs and Bioverativ can select, under one or more license collaborations, products for each program.

Under the Bioverativ agreement, we are obligated to perform research activities on each active research program, under mutually agreed upon research plans. The research and development services for each program (including for clarity the third, optional program) consist of two stages. The first is an initial stage of screening and optimization to identify high affinity Bicycle binders and optimization of early drug like properties and is led by Bicycle. If lead compounds are identified, the second stage includes chemical optimization and testing of these compounds in disease relevant biological assays, conducted jointly by us and Bioverativ, in preparation for lead collaboration product nomination. Each collaboration program has a maximum initial period of three years, unless a program is abandoned or extended for up to one year by Bioverativ. Bioverativ may, at its sole discretion, approve any compound to be progressed into drug development and upon the selection of a collaboration product for each collaboration program, must pay a $5.0 million payment (or $7.0 million if such product includes certain additional enabling intellectual property developed by us in the course of the collaboration) in order to obtain worldwide development and exploitation rights for that collaboration product. Bioverativ will lead preclinical and clinical development, as well as subsequent marketing and commercialization.

Under the terms of the Bioverativ collaboration agreement, we granted to Bioverativ, for each collaboration program, a non-exclusive, sublicensable (through multiple tiers), worldwide license under certain of our intellectual property to conduct the activities assigned to Bioverativ in the applicable research plan for the duration of the applicable research term, but for no other purpose and we have agreed not to, directly or indirectly, by ourselves or in collaboration with others, screen the Bicycle platform for compounds that bind to a target that is the subject of the Bioverativ collaboration or otherwise perform any work related to or disclose such a target until the earliest of the filing acceptance for the first regulatory approval in a major market with respect to the collaboration program, termination or abandonment of such collaboration program or the seventh anniversary of the first date of the research term for the collaboration program.

Under the terms of the Bioverativ collaboration agreement, we received a $10.0 million up front cash payment. Additionally, prior to the initiation of the research plan for each of the first two collaboration programs, Bioverativ made a non-refundable payment of $1.4 million for the sickle cell program and $2.8 million for the hemophilia program as payment for our services during the respective Bicycle Research Term for each program. During the Joint Research Term, Bioverativ is obligated to fund our services at a minimum of $0.7 million and fund certain external costs incurred by us of up to $1.0 million per year. In addition, Bioverativ is required to make certain other milestone payments to us upon the achievement of specified development, regulatory and commercial milestones. More specifically, for each collaboration program, we are eligible to receive, inclusive of the $5.0 to $7.0 million milestone payment described above, between $47.5 million and $67.0 million in development milestone payments. We are also eligible to receive up to $104.0 million in regulatory milestone payments for each collaboration product. In addition, we are eligible to receive up to $55.0 million in commercial milestone payments, on a collaboration program by collaboration program basis. In addition, to the extent any of the collaboration products

covered by the licenses granted to Bioverativ are commercialized, we would be entitled to receive tiered royalty payments of mid-single digits to low-teen digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including for instances where Bioverativ faces generic competition in certain countries.

Either party may terminate the agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. Either party may terminate the agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. In the event of a breach, the collaboration agreement may be terminated by either party in its entirety, or, if the breach is limited to a country or countries, with respect to the country or countries to which the breach applies. Bioverativ may terminate the agreement, entirely or on a program by program, licensed product by licensed product or country by country basis, for convenience.

Bioverativ was also provided with an option to obtain screening services on the additional program upon making an option fee payment in addition to a non-refundable payment as payment for our services during the respective Bicycle Research Term. The option expired in November 2018 unexercised. Bioverativ exercised its right to terminate the sickle cell program in March 2019. The hemophilia program is continuing. We own the material intellectual property rights developed under the sickle cell program and are currently evaluating whether to advance it as an internal program, seek a collaborator or cease work on the program.

AstraZeneca

In November 2016, we entered into a research collaboration agreement with AstraZeneca AB. The collaboration is focused on the research and development of Bicycle peptides that bind to an undisclosed number of biological targets for the treatment of respiratory, cardiovascular and metabolic diseases. After discovery and initial optimization of such Bicycle peptides, AstraZeneca will be responsible for all research and development, including lead optimization and drug candidate selection. AstraZeneca receives development, commercialization and manufacturing license rights with regard to any selected drug candidate(s).

Under the AstraZeneca collaboration agreement, Bicycle is obligated to use commercially reasonable efforts to perform research activities, under mutually agreed upon research plans. The research plans includes two discrete parts, on a research program by research program basis: (i) the Bicycle Research Term, which is focused on the generation of Bicycle peptide libraries using our peptide drug discovery platform, to be screened against selected biological targets, with the goal of identifying compounds that meet agreed criteria set by the parties, and (ii) the AZ Research Term, during which AstraZeneca may continue research activities with the goal of identifying compounds that satisfy the relevant pharmacological and pharmaceutical criteria for clinical testing. AstraZeneca may, at its sole discretion, approve any compound to be progressed into drug development and, upon the selection of each drug candidate, AstraZeneca is to pay a milestone of $8 million.

Each research program is to continue for an initial period of three years, referred to as the research term, including one year for the Bicycle Research Term and two for the AZ Research Term. AstraZeneca may extend the research term for each research program by twelve months (or fifteen months, if needed to complete certain toxicology studies). The research term for a specific program can be shorter if it is ceased due to a screening failure, a futility determination, or abandonment by AstraZeneca. AstraZeneca has certain substitution rights should a screening failure or futility determination be reached. but is obligated to fund these additional efforts related to substitution.

Under the terms of the AstraZeneca collaboration agreement, we granted to AstraZeneca the right and license (with the right to sublicense) to certain background, foreground and platform intellectual property, for the duration of the agreement, to the extent reasonably necessary or useful for AstraZeneca to conduct the activities that are assigned to it in the applicable research plan or that are reasonably necessary or useful or the purpose of researching, developing or exploiting resulting compounds and products. We have agreed not to, directly or indirectly, by ourselves or in collaboration with others, screen the Bicycle platform for compounds that bind to a target that is the subject of the AstraZeneca collaboration or otherwise perform any work related to or disclose such a target until the earlier of the tenth anniversary of the date on which such target was selected or the dosing of the first patient in the first Phase III clinical trial for a product that modulates such collaboration target.

The activities under the AstraZeneca collaboration agreement are governed by a joint steering committee and joint project team each formed by an equal number of representatives from our company and AstraZeneca. The joint steering committee oversees and reviews each research program and the activities of the joint program team. Among other responsibilities, the joint steering committee monitors the research progress and ensures open and frequent exchange between the parties regarding research program activities.

AstraZeneca receives development and commercialization licenses associated with each designated drug candidate, and owes a milestone fee of $8 million for the first drug candidate selected from each research program. In addition, AstraZeneca is required to make certain other milestone payments to us upon the achievement of specified development, regulatory and commercial milestones. More specifically, for each research program, we are eligible to receive, in addition to the milestone fee described above, up to $162 million in development, regulatory and commercial milestones on a research program by research program basis, for a total of up to $170 million in milestone payments per research program. We are eligible to receive these milestone payments for up to six research programs. In addition, to the extent any of the drug candidates covered by the licenses conveyed to AstraZeneca are commercialized, we would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including in certain countries where AstraZeneca faces generic competition. In total, we could receive more than $1 billion in milestone payments and royalties under the collaboration agreement.

Either party may terminate the AstraZeneca collaboration agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. In the event of a breach, the collaboration agreement may be terminated in its entirety, or, if the breach is limited to a country or countries, with respect to the country or countries to which the breach applies. Either party may terminate the AstraZeneca collaboration agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. AstraZeneca may terminate the AstraZeneca collaboration agreement, entirely or on a licensed product by licensed product or country by country basis, for convenience.

Under the AstraZeneca collaboration agreement, AstraZeneca was granted an option to nominate additional targets on the same contractual terms as the initial targets. In May 2018, AstraZeneca made an irrevocable election to exercise the additional target option, giving AstraZeneca the option to designate additional targets, for $5.0 million that was paid by AstraZeneca to us in January 2019.

Oxurion (formerly ThromboGenics)

In August 2013, we entered into a research collaboration and license agreement with Oxurion NV (formerly ThromboGenics NV), or Oxurion. Under the Oxurion collaboration agreement, we are responsible for identifying Bicycle peptides related to the collaboration target, human plasma kallikrein, for use in various ophthalmic indications. Oxurion is responsible for further development and product commercialization after the defined research screening is performed by us.

The collaboration includes two stages. During Stage I, which has been completed, we were obligated to perform specific research activities in accordance with the research plan focused on screening the target using our Bicycle platform to identify compounds that meet the criteria set by the parties. During Stage II, which is ongoing, Oxurion has continued research activities on selected Bicycle peptides with the goal of identifying compounds for further development and commercialization. We are not obligated or expected to perform any research services during Stage II of the research plan. THR-149 has been selected as a development compound under the Oxurion collaboration agreement.

We granted certain worldwide intellectual property rights to Oxurion for the development, manufacture and commercialization of licensed compounds associated with plasma kallikrein.

The Oxurion collaboration agreement provided an upfront payment of €1.0 million and potential additional research and development funding, at an agreed upon FTE rate, should the research effort require more than one FTE or the research plan be amended or extended by Oxurion. In addition, Oxurion is required to make certain milestone payments to us upon the achievement of specified research, development, regulatory and commercial milestones. More specifically, for each collaboration compound, we are eligible to receive up to €8.3 million in research and development milestone payments, from which we have received €1.8 million as of March 31, 2019, in connection with the development of THR-149, and up to €16.5 million in regulatory milestone payments. In addition, to the extent any of the collaboration products covered by the licenses granted to Oxurion are commercialized, we would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Royalty payments are subject to certain reductions. Also, if Oxurion grants a sublicense to a third party for rights to the program for non-ophthalmic use prior to the filing of an IND, we would be entitled to receive payments in the double digits (no higher than first quartile) based on a percentage of non-royalty sublicensing income. If Oxurion grants a sublicense to a third party for rights to the program for non-opthalmic use after the filing of an IND, we would be entitled to receive payments of mid-single digits to low teen-digits.

Either party may terminate the Oxurion collaboration agreement if the other party has breached any of its material obligations and such breach continues after the specified cure period. Either party may terminate the Oxurion collaboration agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party. Oxurion may terminate the Oxurion collaboration agreement for convenience. We may terminate the Oxurion collaboration agreement if Oxurion challenges the validity of any licensed patents or opposes the grant of a licensed patent.

In November 2017, we entered into an amendment to the Oxurion collaboration agreement. This amendment provides for additional research services to be performed by us related to the identification of additional Bicycles binding to the target for Oxurion, in its discretion, to select as development compounds. We were obligated to perform the work in accordance with an amended research plan under Stage I of the collaboration and were funded at a specified FTE rate, plus any direct out of pocket expenses, and Oxurion will be responsible for Stage II research and any development after the selection of a development compound. We completed Stage I of the

research plan during 2018. Additional milestones were added for the potential additional licensed compounds, consistent with those of the initial Oxurion collaboration agreement. Additionally, the tiered royalty rates for all licensed compounds other than THR-149 was increased by one percentage point. We are not obligated or expected to perform any research services during Stage II of the collaboration.

Founder Royalty Arrangements

We have entered into two royalty agreements with our founders, Christian Heinis, John Tite, and Sir Greg Winter, and our initial investors, Atlas Venture Fund VIII LP, Novartis Bioventures LTD. Pursuant to the first royalty agreement, we are obligated to pay an aggregate royalty percentage in the low single digits on net sales arising from products licensed under the Oxurion collaboration agreement. Pursuant to the second royalty agreement, we are obligated to pay an aggregate royalty percentage in the low single digits on net sales arising from products licensed under the AstraZeneca collaboration agreement.

Intellectual Property

Overview

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including our *Bicycle* platform. This includes seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties, which are directed to the use of our Bicycle platform and composition of matter involved in the platform, composition of matter and use of product candidates, and other inventions that are important to our business. We have three patent families directed to novel scaffolds, and 11 patent families directed to our platform technology, including the composition of matter of Bicycle® binders and method of treatment of related indications, including cancer. For example, a patent family directed to the composition of matter of Bicycle® binders and method of treatment of related indications, including cancer, was issued in the United States and Europe, and is pending in several other jurisdictions. The issued patents from this family, and the pending patent applications if issued, are expected to expire in 2034, before patent term extensions, if any. We have 63 patent families directed to the composition of matter of bicyclic peptides and related conjugates, and six patent families directed to methods of using bicyclic peptide conjugates for treating various indications. For example, two patent families directed to the composition of matter of one of our product candidates, BT1718, and methods of use for treating cancer are pending in certain jurisdictions, which if issued, would expire in 2035 and 2037, respectively. We also rely on trade secrets and know-how that may be important for the development of our business. This includes aspects of our proprietary technology platform and our continuing technological innovation to develop, maintain, and strengthen our position in the field of peptide, peptidomimetic, and small molecule-based therapeutics. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our product candidates, technology and know-how, defend and enforce our patents; prevent others from infringing our proprietary rights, preserve the confidentiality of our trade secrets, and to operate without infringing the proprietary rights of others.

Our ability to stop third parties from making, having made, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. In some cases, these rights may need to be enforced by third party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to

any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same. For more information, please see "Risk Factors — Risks Related to Our Intellectual Property."

We seek to protect our proprietary position in a variety of ways, including by pursuing patent protection in certain jurisdictions where it is available. For example, we file U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use specific technologies in our research and development.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application related to the patent. A U.S. patent also may be accorded a patent term adjustment, or PTA, under certain circumstances to compensate for delays in obtaining the patent caused by the United States Patent and Trademark Office. In some instances, such a PTA may result in a U.S. patent term extending beyond 20 years from the earliest date of filing a non-provisional patent application related to the U.S. patent. In addition, in the United States, the term of a U.S. patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

Company-Owned Intellectual Property

As of April 2, 2019, our patent portfolio included three patent families covering novel scaffolds, 11 patent families directed to our platform technology, 63 patent families covering bicyclic peptides and related conjugates, and six patent families directed to clinical indications and other properties of development assets. In total, as of April 2, 2019, we owned 40 patents in the U.S. and in Australia, Canada, China, Europe, Japan, New Zealand, Russia and Singapore, with terms expiring at various dates in February 2029 to October 2034 exclusive of potential patent term adjustment and/or patent term extension.

In addition, as of April 2, 2019, we had 139 patent applications pending in the U.S. and Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, South Korea, New Zealand, Russia and Singapore, and any patents that may be issued from these patent applications are generally expected to have terms that will expire at various dates in February 2029 to April 2040 subject to possible patent term extensions and/or patent term adjustments.

Trade Secret Protection

Finally, we may rely, in some circumstances, on trade secrets to protect our technology. We anticipate relying on trade secrets to protect the know-how behind our *Bicycle* platform. However, trade secrets can be difficult to protect. We seek to protect our technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For further information, please see "Risk Factors — Risks Related to Our Intellectual Property."

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are a number of currently marketed products and product candidates in preclinical research and clinical development by third parties for the various oncology applications that we are targeting. For example, a number of multinational companies as well as large biotechnology companies, including Astellas Pharma, Inc., Seattle Genetics, Inc., AstraZeneca, and GlaxoSmithKline plc, are developing programs for the targets that we are exploring for our BTC programs. Furthermore, Agenus Inc., Bristol-Myers Squibb Company, Pfizer Inc., and Roche Holding AG, or Roche, have or are developing programs for CD137, and Amgen Inc., Pieris Pharmaceuticals, Inc. and Roche are developing bi-specifics. In addition, we are aware that technologies for drug discovery, including peptide-based medicines, continue to advance rapidly, which may compete with our own screening technology or render it obsolete.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in discovering product candidates, obtaining approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

Sales and Marketing

Subject to receiving marketing approval, we intend to pursue the commercialization of our product candidates either by building internal sales and marketing capabilities or through opportunistic collaborations with others.

We plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Manufacturing

Each of our *Bicycles* is entirely synthetic. We believe the synthetic nature of our product candidates allow for a more cost effective and scalable manufacturing process compared to biologics. In addition, this property of *Bicycles* allows for the manufacturing of product candidates of consistent pharmaceutical quality with favorable stability characteristics. Based on our experience, we believe that the manufacturing of *Bicycles* can be made to be well controlled, reproducible and scalable.

We operate an outsourced model for the manufacture of our product candidates, and contract with good manufacturing practice, or GMP, licensed pharmaceutical contract development and manufacturing organizations, both for the synthesis of each drug substance component, and the formulation and packaging of the finished drug product. We selected these organizations based on their experience, capability, capacity and regulatory status. We do not own or operate GMP manufacturing facilities, nor do we currently plan to build our own GMP manufacturing capabilities for the production of candidates for clinical or commercial use.

We currently engage five third-party manufacturers to provide clinical supplies of our product candidates, three third-party manufacturers to provide non-clinical supplies of our product candidates and three third-party manufacturers to provide fill-finish services. Projects are managed by a specialist team of our internal staff, which is designed to promote compliance with the technical aspects and regulatory requirements of the manufacturing process.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs and devices under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product seizures,

total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities. In addition, an applicant may need to recall a product.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent IRB representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study

protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA can place an IND on full or partial clinical hold at any point in development, and depending upon the scope of the hold, clinical trial(s) may not restart until resolution of the outstanding concerns to the FDA's satisfaction.

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- ***Phase I.*** The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- ***Phase II.*** The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- ***Phase III.*** The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

- ***Phase IV.*** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase I, Phase II and Phase III clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the applicant must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to substantial user fees, and the sponsor of an approved NDA is also subject to annual program user fees. These fees are typically increased annually.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are Fast Track designation, Breakthrough Therapy designation and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that is expected to lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase IV or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information,

the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase IV clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program user fee requirements for any marketed products, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the NDA holder and any third-party manufacturers that the NDA holder may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or voluntary product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs generally may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Companion Diagnostics

We may employ companion diagnostics to help us to more accurately identify patients within a particular subset, both during our clinical trials and in connection with the commercialization of our product candidates that we are developing or may in the future develop. Companion diagnostics can identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA and, as such, require either clearance or approval prior to commercialization. The level of risk combined with available controls to mitigate risk determines whether a companion diagnostic device requires Premarket Approval Application, or PMA, approval or is cleared through the 510(k) premarket notification process. For a novel therapeutic product for which a companion diagnostic device is essential for the safe and effective use of the product, the companion diagnostic device should be developed and approved or 510(k)-cleared contemporaneously with the therapeutic. The use of the companion diagnostic device will be stipulated in the labeling of the therapeutic product.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic

equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, which states the proposed generic drug will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. An applicant who submits a section 505(b)(2) NDA, which is for new or improved formulations or new uses of previously approved drug products and where at least one or more of the investigations relied upon by the applicant for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted, also must certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a

patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures

relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Amendments, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Europe/Rest of World Regulation

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of products, if approved. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the clinical trial application is approved in accordance with a country's requirements, clinical trial development may proceed. To obtain regulatory approval of an investigational drug under EU regulatory systems, a manufacturer must submit a marketing authorization application. More concretely, in the EEA (which is comprised of the 28 Member States of the EU plus Norway, Liechtenstein and Iceland, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as

biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

In Europe, the period of orphan drug exclusivity is ten years, although it may be reduced to six years if, at the end of the fifth year, it is established that the criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product approval, pricing and reimbursement vary from country to country. In all cases, the clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. Additionally, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, no uniform policy for coverage and reimbursement exists in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations.

Therefore one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for our product candidates will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Other Healthcare Laws and Regulations

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted regulatory approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Such restrictions under applicable federal and state healthcare laws and regulations, include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting and physician sunshine laws. Some of our pre-commercial activities are subject to some of these laws.

The federal Health Care Program Anti-Kickback Statute, or Anti-Kickback Statute, prohibits any person or entity, including a prescription drug manufacturer or a party acting on its behalf, from, among other things, knowingly and willfully, directly or indirectly, soliciting, receiving, offering, or providing any remuneration that is intended to induce the referral of business, including the purchase, order or recommendation or arranging of, any good or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Moreover, a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent or not provided as claimed. Persons and entities can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, any of our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and other third-party payor reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Penalties for federal civil False Claims Act violations may include up to three times the actual damages sustained by the government, plus significant mandatory civil penalties for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, False Claims Act violations may also implicate various federal criminal statutes.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that any of our product candidates, if approved, are sold in a foreign country, we may be subject to similar foreign laws.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, defined as independent contractors or agents of certain healthcare providers, healthcare clearinghouses and health plans, known as covered entities, that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities and business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, certain state and foreign laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The U.S. federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, ACA, , including the provision commonly referred to as the Physician Payments Sunshine Act imposed, among other things, new annual reporting requirements for covered manufacturers for certain payments and other transfers of value provided to physicians and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, covered manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties of up to an aggregate of over $169,000 per year and up to an aggregate of over $1.1 million per year for "knowing failures." Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices or require the tracking and reporting of gifts, compensation or other remuneration to physicians.

Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we intend to develop a comprehensive compliance program that establishes internal control to facilitate adherence to the rules and program requirements to which we will or may become subject. Although the development and implementation of compliance programs designed to establish internal control and facilitate compliance can mitigate the risk of investigation, prosecution, and penalties assessed for violations of these laws, the risks cannot be entirely eliminated.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, including Medicare and Medicaid, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Healthcare Reform

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress passed the ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of the types of entities eligible for the 340B drug discount program;
- establishment of the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing or delaying penalties, starting January 1, 2019, for not complying with the Affordable Care Act's individual mandate to carry health insurance, delaying the implementation of certain ACA-mandated

fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. For example, in November 2018, CMS issued a proposed rule for comment that would, among other things, provide Medicare prescription drug plans under Part D more transparency in pricing and greater flexibility to negotiate discounts for, and in certain circumstances exclude, drugs in the six "protected" formulary classes and allow Medicare Advantage plans to use certain drug management tools such as step therapy for physician-administered drugs. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Employees

As of May 1, 2019, we had 61 full-time or part-time employees, including 28 with M.D. or Ph.D. degrees. Of these employees, 51 employees are engaged in research and development activities and 10 employees are engaged in general and administrative activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider the relationship with our employees to be good.

Facilities

We occupy approximately 13,500 rentable square feet of office and laboratory space in Cambridge, United Kingdom under a lease that expires in December 2021, with a five-year extension option, and an additional 11,000 rental square feet of office and laboratory space in Lexington, Massachusetts under a lease that expires in December 2022, with a five-year extension option. We believe that our office and laboratory spaces are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Legal Proceedings

Other than as described below, we are not currently subject to any material legal proceedings.

License Litigation

In 2009, we entered into a non-exclusive patent license agreement with Pepscan Systems B.V., or Pepscan, pursuant to which we licensed rights related to the scaffold used for *Bicycles* contained in certain of our product candidates, including our lead product candidate, BT1718. The agreement required us to enter into a framework services agreement with Pepscan for Pepscan to provide certain *Bicycles* not produced by us. In 2010, we entered into such a framework services agreement. In 2014, we terminated the framework services agreement in accordance with its terms. Subsequently, in 2016, Pepscan terminated the patent license agreement.

We instituted proceedings in the District Court of The Hague to contest the right of Pepscan to terminate the patent license agreement. In response, Pepscan claimed, among other things, that the termination of the framework services agreement and alleged breaches by us of confidentiality obligations constituted grounds for the termination of the patent license agreement. In a preliminary judgement delivered in April 2018, the District Court of the Hague rejected Pepscan's claim that it was entitled to terminate the patent license agreement on the basis of a breach of a purported exclusive supply obligation. The District Court of the Hague reserved for further proceedings the question of whether Pepscan was entitled to terminate the patent license agreement on the basis of allegations that we had breached our confidentiality obligations. The District Court of the Hague gave us an opportunity to submit proof to the contrary through written evidence and further hearings.

In July 2018, Pepscan appealed the decision of the District Court of the Hague and the proceedings before the District Court of the Hague have been stayed pending a decision in the appeal brought by Pepscan. We intend to defend the appeal and any further proceedings before the District Court of the Hague.

The patent that is the subject of these proceedings expires in 2024.

European Patent Opposition Proceedings

In January 2013, Pepscan filed a notice of opposition in respect of European patent 2 257 624, which is a foundational patent that covers our technology platform. In June 2015, the European Patent Office issued a decision to maintain this patent as granted and rejecting Pepscan's opposition. Pepscan subsequently filed a notice of appeal to revoke the patent in its entirety, along with supporting materials. We filed a reply requesting that the appeal be dismissed. As of the date of this prospectus, no decision has been issued by the European Patent Office in respect of this appeal.

In April 2015, Pepscan filed a notice of opposition in respect of European patent 2 474 613, which is a divisional patent that covers extensions of our technology platform. In February 2017, the European Patent Office issued a decision to maintain this patent in its amended form, which upheld

this patent. Pepscan subsequently filed a notice of appeal to revoke the patent in its entirety, along with supporting materials. We also filed a Notice of Appeal contesting the amendments to the patent required by the decision of the Opposition Division along with supporting materials. As of the date of this prospectus, no decision has been issued by the European Patent Office in respect of these appeals.

MANAGEMENT

Executive Officers and Directors

Our executive officers and directors and their respective ages and positions as of May 1, 2019:

Name	Age	Position(s)
Executive Officers:		
Kevin Lee, Ph.D., MBA	51	Chief Executive Officer and Director
Lee Kalowski, MBA	38	President and Chief Financial Officer
Peter Leone, MBA	62	Chief Business Officer
Michael Skynner, Ph.D.	50	Chief Operating Officer
Nick Keen, Ph.D.	51	Chief Scientific Officer
Non-Employee Directors		
Pierre Legault, MBA, CPA	59	Director and Non-Executive Chairman of the Board of Directors
Michael Anstey, DPhil[1][3]	38	Director
Kate Bingham, MBA[1]	53	Director
Deborah Harland, Ph.D., MBA[2][3]	58	Director
Anja König, Ph.D.	48	Director
Eashwar Krishnan*	42	Director
Carolyn Ng, Ph.D.[1][2]	35	Director
Jason Rhodes, MBA	49	Director
Sir Greg Winter, FRS	68	Director
Director Nominee		
Bosun Hau, MBA*	40	Director Nominee

* Upon effectiveness of the registration statement of which this prospectus forms a part, Mr. Krishnan will resign as a member of our board of directors, and Mr. Hau will become a member of our board of directors.

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Corporate Governance Committee.

The following is a biographical summary of the experience of our executive officers and directors. There are no family relationships among any of our executive officers or directors.

Executive Officers

Kevin Lee, Ph.D., MBA has served as our Chief Executive Officer and a member of our board of directors since September 2015. From April 2012 to September 2015, Dr. Lee served as Senior Vice President and Chief Scientific Officer of the Rare Disease Research Unit at Pfizer Inc., a pharmaceutical company. From November 2004 to April 2012, Dr. Lee worked at GlaxoSmithKline plc, where in addition to leading the formation of multiple strategic commercial and academic partnerships, he led epigenetics research and was responsible for the creation of the EpiNova Discovery Performance Unit. Before joining GlaxoSmithKline, Dr. Lee was a lecturer at Warwick University Medical School and founded Cambridge Biotechnology Ltd, which specialized in developing small molecule and peptide therapeutics for inflammation and metabolic diseases before its trade sale to Biovitrum in 2005 and Neurosolutions (now Oncosil Medical Ltd ASX). Dr. Lee received a BPharm from Nottingham University and a Ph.D. in pharmacology from Cambridge University. Dr. Lee has an MBA from Warwick Business School and currently serves as

a non-executive director for Nodthera Ltd, a position he has held since October 2018, and as a director at Wilbraham Consulting Ltd., a position he has held since December 2017.

We believe that Dr. Lee is qualified to serve on our board of directors based on his extensive leadership, executive, managerial, business and pharmaceutical and biotechnology company experience, along with his years of industry experience in the development and commercialization of pharmaceutical products.

Lee Kalowski, MBA has served as our Chief Financial Officer since July 2017 and as our President since January 2019. Prior to joining us, from September 2014 until September 2016, Mr. Kalowski served as the Chief Financial Officer and from September 2016 until May 2017, served as the consulting Chief Financial/Business Officer of Tokai Pharmaceuticals, Inc. (NASDAQ: TKAI), a biopharmaceutical company. Prior to Tokai, from June 2010 to September 2014, Mr. Kalowski served in global biotechnology equity research at Credit Suisse, where he covered companies in the biopharmaceutical industry as a Senior Analyst from May 2011 until September 2014 and as an Associate from June 2010 until May 2011. Mr. Kalowski received a B.A. in biology and economics from Union College and an MBA from The Wharton School of the University of Pennsylvania.

Peter Leone, MBA has served as our Chief Business Officer since February 2019. Prior to joining us, from May 2016 to January 2019, Mr. Leone served as Vice President of Strategic Business Initiatives and from April 2012 to May 2016, served as Vice President of Strategy and Program Management at Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR), a biopharmaceutical company. Prior to Arrowhead, from 2010 to 2012, Mr. Leone was Chief Operating Officer at Alvos Therapeutics, Inc., a biopharmaceutical company, which now operates as a subsidiary of Arrowhead. Before Alvos, Mr. Leone was the founding Chief Executive Officer or Chief Operating Officer at three different venture backed companies, including Mersana Therapeutics, Inc. (NASDAQ: MRSN), a biopharmaceutical company. Mr. Leone received a B.A. in engineering science with pre-med studies from Dartmouth College and an MBA from the Stanford University Graduate School of Business.

Michael Skynner, Ph.D. has served as our Chief Operating Officer since January 2018 and prior to this, served as our Vice President of Operations since January 2016. Prior to joining us, Dr. Skynner worked at Pfizer Inc., a pharmaceutical company, from September 2013 to January 2016, where he was Head of Rare Disease Alliances, led rare disease efforts in Europe and founded and ran the Pfizer Rare Disease Consortium. Prior to Pfizer, from May 2008 to September 2013, Dr. Skynner worked at GlaxoSmithKline plc, where he focused on developing therapeutics targeting inflammatory kinases. Prior to GlaxoSmithKline, in 2001, Dr. Skynner co-founded Cambridge Biotechnology Ltd, which specialized in developing small molecule and peptide therapeutics for inflammation and metabolic diseases before its trade sale to Biovitrum in 2005. Dr. Skynner obtained his Ph.D. in biochemistry from Imperial College.

Nicholas Keen, Ph.D. has served as our Chief Scientific Officer since January 2017. Prior to joining us, from April 2011 until December 2016, Dr. Keen was the Head of Oncology Drug Discovery at the Cambridge (US) office of the Novartis Institutes for Biomedical Research (NIBR), a subsidiary of Novartis AG, a pharmaceutical company. Prior to Novartis, from August 2005 to March 2011, Dr. Keen led the early lead generation group for oncology at AstraZeneca plc's US research site in Waltham, MA, and before this, from January 1997 to July 2005 worked in AstraZeneca's UK oncology research group. Dr. Keen completed his undergraduate studies at the University of Cambridge, his graduate studies at the Imperial Cancer Research Fund in Cambridge and his post-doctoral studies at the Laboratory of Molecular Biology in Cambridge.

Non-Employee Directors

Pierre Legault, MBA, CPA has served as our chairman and a member of our board of directors since March 2019. Mr. Legault has served on the board of directors of Urovant Sciences Ltd. since July 2018 and has also served on the board of directors of Poxel SA since January 2016 and has been chairman of such board since March 2016. Since February 2018, Mr. Legault has served on the board of directors and as chairman of the board of Artios Pharma Limited. Mr. Legault has also served as a director of Clementia Pharmaceuticals Inc. since January 2018 and Syndax Pharmaceuticals Inc. since January 2017. Mr. Legault has also previously served as a member of the boards of directors at Forest Laboratories, Inc., Tobira Therapeutics, Inc., NPS Pharmaceuticals, Inc., Regado Biosciences, Inc., ARMO Biosciences, Inc., Iroko Pharmaceuticals LLC, Cyclacel Pharmaceuticals Inc., Eckerd Pharmacy and NephroGenex, Inc., where he also served as the Chairman and Chief Executive Officer from 2012 to 2016. From 2010 to 2012, Mr. Legault served as the Chief Executive Officer of Prosidion Ltd., a subsidiary of Astellas Pharma Inc., and from 2009 to 2010, he served as the Chief Financial Officer and Treasurer of OSI Pharmaceuticals, Inc. Mr. Legault also previously served as the Chief Executive Officer of Eckerd Pharmacy and Senior Executive Vice President and Chief Accounting Officer of the Rite Aid Corporation. Between 1989 and 2005, Mr. Legault held various global roles such as President, Chief Executive Officer and Chief Financial Officer at legacy companies of the Sanofi-Aventis group. Mr. Legault earned a B.B.A. in Business & International Finance from HEC Montreal, an MBA. in Marketing from McGill University and holds C.A. and C.P.A. diplomas. He also studied at Harvard Business School in their Graduate Executive MBA program.

We believe that Mr. Legault's is qualified to serve on our board of directors based on his experience leading and managing a number of biopharmaceutical companies.

Michael Anstey, DPhil has served as a member of our board of directors since June 2017. Dr. Anstey is an Investment Director at Cambridge Innovation Capital plc. Prior to this role, from January 2010 to January 2017, Dr. Anstey was a Principal in the Healthcare Practice Area of the Boston Consulting Group. Prior to Boston Consulting Group, Inc., from January 2008 to December 2009, Dr. Anstey was on the investment team at Oxford Capital Partners LLP. Dr. Anstey currently serves on the board of directors of Congenica Ltd. and Storm Therapeutics Ltd. Dr. Anstey graduated with a first class honors degree in biology from Queen's University, Canada and earned a DPhil in zoology in the field of neurobiology from Oxford University.

We believe that Dr. Anstey is qualified to serve on our board of directors based on his knowledge of the healthcare sector and his experience as a seasoned investor.

Kate Bingham, MBA has served as a member of our board of directors since October 2014. Ms. Bingham joined SV Health Investors (then Schroder Ventures), a venture capital fund, in 1991. Ms. Bingham currently serves on the boards of directors of Autifony Therapeutics Limited, Calchan Holdings Limited, Karus Therapeutics Limited, Ervaxx Limited, TRex Bio, Zarodex Therapeutics Limited, Pulmocide Limited and Sitryx Therapeutics Limited. She is Deputy Chairman of St. Paul's Girls' School, London, and sits on the Investment Committee of Oxford University Spin-out Equity Management (OSEM). Ms. Bingham holds a B.A. in biochemistry from Oxford University and graduated from Harvard Business School with an MBA.

We believe that Ms. Bingham is qualified to serve on our board of directors based on her knowledge of the healthcare sector across international markets.

Deborah Harland, Ph.D., MBA has served as a member of our board of directors since December 2009. Since 2005, Dr. Harland has been a Partner at S.R. One, Limited, the corporate venture capital arm of GlaxoSmithKline plc. Dr. Harland is currently a member of the boards of directors of Asceneuron SA, F-star, MISSION Therapeutics Ltd., and VHsquared Ltd. and is an

independent Director on the Board of Cancer Research Technology, the specialist commercialisation and development arm of Cancer Research UK, the world's largest cancer research charity. Dr. Harland holds a BSc. (with honors) in pharmacology from the University of Bath, a Ph.D. in pharmacology from the University of London and an MBA from Henley Management College.

We believe that Dr. Harland is qualified to serve on our board of directors based on her knowledge of the healthcare sector across international markets, her extensive operational, drug development and licensing experience.

Anja König, Ph.D. has served as a member of our board of directors since 2009. Dr. König is the global head of the Novartis Venture Fund in Basel, Switzerland. Dr. König currently serves on the board of directors of Forendo Pharma, Ltd. Prior to joining Novartis in 2006, she was an Associate Partner at McKinsey & Company, where she was a leader in McKinsey's North American Pharmaceutical Practice. Dr. König holds a Ph.D. in physics from Cornell University.

We believe Dr. König's extensive knowledge of the healthcare sector qualifies her to serve on our board of directors. Dr. König has notified us that she will resign from our board of directors immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. Dr. König's resignation is not due to any disagreement with the company or any matters relating to our operations, policies or practices.

Eashwar Krishnan has served as a member of our board of directors since 2019. Mr. Krishnan is the Managing Partner of Tybourne Capital Management, a Hong Kong based global equity investment management firm founded in 2012. Prior to founding Tybourne, Mr Krishnan was a senior analyst at Lone Pine Capital for over 11 years. Mr. Krishnan joined Lone Pine Capital in 2000 as a Managing Director with responsibility for the firm's global technology investments. Prior to joining Lone Pine Capital, Mr Krishnan spent two years as an analyst in the Principal Investment Area at Goldman Sachs in London (1998-2000) and worked as a summer research fellow at the Jet Propulsion Laboratory in Pasadena, California (1997). Mr Krishnan holds a first class degree in Physics from Trinity College, Cambridge University, U.K. and St. Stephen's College, Delhi University, India. Mr. Krishnan also serves on the Campaign Board of Cambridge University.

We believe Mr. Krishnan is qualified to sit on our board of directors based on his extensive investment experience, including in the life sciences.

Carolyn Ng, Ph.D. has served as a member of our board of directors since 2018. Dr. Ng is a principal of Vertex Ventures HC, a global venture capital firm. Dr. Ng currently serves on the Board of Obsidian Therapeutics, Inc. and Twentyeight-Seven Therapeutics, Inc. Prior to joining Vertex, from 2012 to 2014, Dr. Ng was a Pharma Strategy Consultant at Deallus Consulting, a specialized life sciences consulting firm. Dr. Ng started her career in the oncology pharmacy department of the National University Cancer Institute of Singapore, where she worked in 2006. Dr. Ng holds a Ph.D. in Cancer Molecular Biology from the National University of Singapore Graduate School for Integrative Sciences and Technology and a B.S. degree in pharmacy with first class honours from the National University of Singapore.

We believe that Dr. Ng is qualified to serve on our board of directors based on her extensive experience in life sciences investing and knowledge of the healthcare sector.

Jason Rhodes, MBA has served as a member of our board of directors since 2015. Mr. Rhodes is a partner at Atlas Venture LP, a venture capital firm, since 2014. He has been a Founder and Chairman of Generation Bio, Co. since 2016 and a Founder, Chairman and currently acting Chief Executive Officer of Disarm Therapeutics, Inc. since 2016, both of which are biotechnology companies. He has been a member of the boards of directors of Replimune Group, Inc. (NASDAQ: REPL) since 2015, Gemini Therapeutics, Inc. since 2016 and Accent

Therapeutics, Inc. since 2017. From 2010 to 2014, Mr. Rhodes was at Epizyme, Inc. (NASDAQ: EPZM), where he most recently served as President and Chief Financial Officer. He led business development at Alnylam (NASDAQ: ALNY) from 2007 to 2010. Mr. Rhodes obtained a B.A. from Yale University in 1991 and an M.B.A. from the Wharton School of the University of Pennsylvania in 1996.

We believe that Mr. Rhodes is qualified to serve on our board of directors based on his experience as a life sciences investor, including serving on other boards of directors. Mr. Rhodes has notified us that he will resign from our board of directors immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. Mr. Rhodes' resignation is not due to any disagreement with the company or any matters relating to our operations, policies or practices.

Sir Greg Winter, FRS is our Co-Founder and has served on of our board of directors since our inception. Sir Greg was a member of staff of the Medical Research Council Laboratory of Molecular Biology (LMB) in Cambridge, U.K from 1981 to 2012, serving as both Deputy and Acting Director. He is currently Master of Trinity College, Cambridge. Sir Greg is a Fellow of the Royal Society and was knighted in 2004 for services to science. In 2018, Sir Greg was awarded a Nobel Prize in Chemistry for his work in developing phage display for the directed evolution of antibodies and peptides to produce new medicines. He has been the Acting Chairman of Biosceptre International Limited from 2016 to 2018. Sir Greg was a founder and non-Executive Director of Cambridge Antibody Technology and Domantis.

We believe that Sir Greg is qualified to serve on our board of directors based on his extensive research experience, knowledge of antibody medicines and academic achievements, combined with his experience in the biotechnology industry.

Director Nominee

Bosun Hau, ***MBA*** is a nominee for appointment to our board of directors, and such appointment will be effective upon effectiveness of the registration statement of which this prospectus forms a part. Since April 2019, Mr. Hau has served as the Managing Director and Co-Head of Private Equity at Tybourne Capital Management, a Hong Kong based global equity investment management firm. Prior to joining Tybourne, from October 2015 to April 2019, Mr. Hau served as a Managing Director and Partner of Sailing Capital in Hong Kong, a global private equity firm. From August 2009 to October 2015, Mr. Hau served as a Partner of MVM Life Science Partners LLP, a venture capital firm. From 2008 to 2009, Mr. Hau served as a management consultant with McKinsey & Company in Southeast Asia and as an early stage venture capital investor with S.R. One Ltd, GlaxoSmithKline's corporate venture group. From July 2004 to August 2007, Mr. Hau served as an equity research analyst covering the medical device and pharmaceutical industries for JP Morgan Securities, Inc. and Prudential Securities, Inc. Mr. Hau is currently a member of the boards of directors of Evolus, Inc., Cellular Biomedicine Group, Inc., ALPHAEON Corporation and Elcelyx Therapeutics Inc., and is a Board Overseer of Beth Israel Deaconess Medical Center in Boston, a major teaching hospital of Harvard Medical School. Mr. Hau received a B.S. in Molecular and Cellular Biology, a B.S.H.S. in Physiological Sciences and a B.A. in Psychology from the University of Arizona, an M.Sc. in Biotechnology from Johns Hopkins University and an M.B.A in Finance and Health Management from the Wharton School at the University of Pennsylvania.

We believe Mr. Hau's extensive experience in the venture capital, private equity and financial services industries qualifies him to serve on our board of directors.

Composition of Our Board of Directors

Our board of directors currently consists of ten members, all of whom were elected pursuant to the board composition provisions of in our articles of association and investment agreement, which is described under "Certain Relationships and Related Party Transactions—Agreements with Our Shareholders" in this prospectus. These board composition provisions will terminate upon the closing of this offering as the articles of association adopted by us immediately prior to closing of this offering will not include such provisions and the investment agreement relating to the group will terminate immediately prior to closing. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and governance committee and board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity and is not limited to race, gender or national origin. We have no formal policy regarding board diversity. Our nominating and governance committee's and board of directors' priority in selecting board members is identification of persons who will further the interests of our shareholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal.

At every subsequent annual general meeting any director who either (i) has been appointed by the board of directors since the last annual general meeting or (ii) was not appointed or reappointed at one of the preceding two annual general meetings, must retire from office and may offer themselves for reappointment by the shareholders by ordinary resolution. See "Description of Share Capital and Articles of Association—Post-IPO Articles of Association—Board of Directors."

Our board of directors has determined that all members of the board of directors, except Kevin Lee, Pierre Legault and Sir Greg Winter are independent, as determined in accordance with the rules of Nasdaq. In making such independence determination, our board of directors considered the relationships that each such non-employee director has with us and all other facts and circumstances that the board of directors deemed relevant in determining their independence. Upon the effectiveness of the registration statement of which this prospectus forms a part, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of Nasdaq and the rules and regulations of the SEC.

Staggered Board

Our articles of association to be effective upon completion of this offering provide that our board of directors will be divided into three classes, Class I, Class II and Class III, each of which will consist, as nearly as possible, of one-third of the total number of directors constituting our entire board and which will serve staggered three-year terms. At each annual general meeting, the successors of directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election.

- Our Class I directors will be Sir Greg Winter and Deborah Harland;
- Our Class II directors will be Kate Bingham, Michael Anstey and Kevin Lee; and
- Our Class III directors will be Carolyn Ng, Bosun Hau and Pierre Legault.

Our articles of association to be effective upon completion of this offering provide that the authorized number of directors may be changed only by ordinary resolution of the shareholders. Any additional directorships resulting from an increase in the number of directors will be distributed

among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent shareholder efforts to effect a change of our management or a change in control.

Board's Role in Risk Oversight

Our board of directors oversees the management of risks inherent in the operation of our business and the implementation of our business strategies. Our board of directors performs this oversight role by using several different levels of review. In connection with its reviews of our operations and corporate functions, our board of directors addresses the primary risks associated with those operations and corporate functions. In addition, our board of directors reviews the risks associated with our business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

Each of our board committees also oversees the management of our risk that falls within the committee's areas of responsibility.

In performing this function, each committee has full access to management, as well as the ability to engage advisors. Our Chief Financial Officer reports to the audit committee and is responsible for identifying, evaluating and implementing risk management controls and methodologies to address any identified risks. In connection with its risk management role, our audit committee meets privately with representatives from our independent registered public accounting firm and our Chief Financial Officer. The audit committee oversees the operation of our risk management program, including the identification of the primary risks associated with our business and periodic updates to such risks, and reports to our board of directors regarding these activities.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates pursuant to a separate charter adopted by our board of directors. The composition and functioning of all of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, Nasdaq and SEC rules and regulations.

Audit Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, Michael Anstey, Kate Bingham and Carolyn Ng will serve on the audit committee, which will be chaired by Michael Anstey. Our board of directors has determined that each member of the audit committee is "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable rules of Nasdaq. Our board of directors has designated Kate Bingham as an "audit committee financial expert," as defined under the applicable rules of the SEC. The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;

- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon the audit committee's review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by the SEC rules to be included in our annual proxy statement;
- reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing earnings releases.

Compensation Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, Deborah Harland and Carolyn Ng will serve on the compensation committee, which will be chaired by Deborah Harland. Our board of directors has determined that each member of the compensation committee is "independent" as that term is defined in the applicable rules of Nasdaq. The compensation committee's responsibilities include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer and Chief Financial Officer;
- evaluating the performance of our Chief Executive Officer and Chief Financial Officer in light of such corporate goals and objectives and recommending or determining the compensation of our Chief Executive Officer;
- reviewing and recommending or determining the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential current compensation advisors in accordance with the independence standards identified in the applicable rules of the Nasdaq Stock Market;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation;
- preparing the compensation committee report required by the SEC rules to be included in our annual proxy statement;

- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K; and
- reviewing and discussing with the board of directors corporate succession plans for the Chief Executive Officer and other key officers.

Nominating and Corporate Governance Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, Michael Anstey and Deborah Harland will serve on the nominating and corporate governance committee, which will be chaired by Deborah Harland. Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as that term is defined in the applicable rules of Nasdaq. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by shareholders;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a set of corporate governance guidelines; and
- overseeing the evaluation of the board of directors and management.

Our board of directors may establish other committees from time to time.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Corporate Governance

We intend to adopt, effective upon the effectiveness of the registration statement of which this prospectus forms a part, a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Following the completion of this offering, a current copy of the code will be posted on the Corporate Governance section of our website, which is located at *www.bicycletherapeutics.com*. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE COMPENSATION

Executive Compensation Overview

Historically, our executive compensation program has reflected our growth and development-oriented corporate culture. To date, the compensation of the other executive officers identified in the summary compensation table below, who we refer to as the named executive officers, has consisted of a combination of base salary, bonuses and long-term incentive compensation in the form of share options or restricted shares. Our executive officers and all salaried employees are also eligible to receive health and welfare benefits.

As we transition from a private company to a publicly-traded company, we will evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require. At a minimum, we expect to review executive compensation annually with input from a compensation consultant if and when determined appropriate by the compensation committee. As part of this review process, we expect the board of directors and the compensation committee to apply our values and philosophy, while considering the compensation levels needed to ensure our executive compensation program remains competitive. We will also review whether we are meeting our retention objectives and the potential cost of replacing a key employee.

Summary Compensation Table — 2018

The following table presents information regarding the total compensation awarded to, earned by, and paid to our principal executive officer and the two most highly-compensated executive officers (other than the principal executive officer) who were serving as our executive officers at the end of the last completed fiscal year for services rendered in all capacities to us. We refer to these individuals as our named executive officers. Our named executive officers for 2018 are:

- Kevin Lee, our Chief Executive Officer;
- Lee Kalowski, our Chief Financial Officer and President; and
- Maria Koehler, our Chief Medical Officer (who resigned from our company in April 2019).

The following table provides information regarding the total compensation, for services rendered in all capacities, that was earned by our named executive officers during the year ended December 31, 2018.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Non-Equity Incentive Plan Compensation ($)	All Other Compensation ($)	Total ($)
Kevin Lee, Ph.D., MBA *Chief Executive Officer*	2018[1]	385,549[2]	127,630[3]	267,904[4]	36,811[5]	817,894
Lee Kalowski, MBA *Chief Financial Officer and President*	2018	349,520[6]	60,000[7]	110,536[4]	—	520,056
Maria Koehler, M.D., Ph.D. *Chief Medical Officer*	2018	385,500[8]	—	127,215[4]	—	512,715

(1) The amounts reported for Dr. Lee have been converted from GBP to USD using an exchange rate of $1.2763 to £1.00 as of December 31, 2018. In December 2018, Dr. Lee surrendered his vested share options in exchange for ordinary shares at a subscription price of £0.01 per ordinary share and surrendered his unvested share options in exchange for a new option grant on the same terms and vesting schedule as the unvested surrendered options. There was no value attributed to either action based on Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 718 and accordingly, there is no amount reported in this table in connection with such award. The assumptions used in calculating the grant date fair value of the shares are set forth in the Notes to our Consolidated Financial Statements included elsewhere in this prospectus.

(2) In 2018, Dr. Lee's base salary was $375,000 and increased in August 2018 to $429,597.

(3) The amount reported reflects a retention bonus paid to Dr. Lee in 2018 that is repayable in full to us if Dr. Lee gives notice prior to August 1, 2020.

(4) The amount reported represents the named executive officer's respective 2018 target bonus that was paid in February 2019, based on achievement of personal and Company goals. With respect to Dr. Lee, the amount also includes a stock grant awarded to Dr. Lee in lieu of cash with a grant date fair value of $24,042 in connection with entering into the Bioverativ collaboration arrangement.

(5) The amounts reported represent relocation reimbursements and $34,937 provided to Dr. Lee for pension benefits.

(6) At the beginning of 2018, Mr. Kalowski's base salary was $340,000 and increased in mid-January 2018 to $349,520.

(7) The amount reported represents a relocation bonus in the amount of $30,000 provided to Mr. Kalowski in 2018 and a discretionary cash bonus in the amount of $30,000 earned by Mr. Kalowski in 2018.

(8) At the beginning of 2018, Dr. Koehler's base salary was $375,000 and increased in mid-January 2018 to $385,500. Dr. Koehler resigned from all positions with our company effective April 30, 2019.

Recent Developments Regarding Executive Compensation

Upon effectiveness of the registration statement of which this prospectus forms a part, we intend to grant options to purchase an aggregate of 1,311,061 ordinary shares to our executive officers at the initial public offering price.

Employment Agreements with Our Named Executive Officers

Kevin Lee, Ph.D. MBA. We will enter into an employment agreement with Dr. Lee, or the Lee Employment Agreement, which will be effective upon closing of this offering. Pursuant to the terms of the Lee Employment Agreement, Dr. Lee will continue to serve as our Chief Executive Officer. Dr. Lee will receive a salary of $575,000, which is subject to review and adjustment in accordance with our policy. Dr. Lee is eligible for an annual discretionary bonus, of up to 50% of his salary, which may be paid in cash, in whole or in part, or options to purchase our shares, based on the achievement of certain performance goals, including corporate objectives, strategic initiatives and regulatory and clinical milestones, as determined by our remuneration committee. Dr. Lee is eligible to participate in our employee benefit plans generally available to our executive employees, subject to the terms of those plans. Dr. Lee's employment may be terminated by either party giving three months notice to the other. However, if we terminate Dr. Lee's employment without Cause or if Dr. Lee terminates the Lee Employment Agreement for Good Reason (as defined in the Lee Agreement) then he is entitled to a severance payment equal to (a) 12 months salary or (b) if within 12 months of a change in control (as defined in the Lee Agreement) 18 months salary and on-target bonus and accelerated vesting and exercise of equity awards, in each case subject to Dr. Lee (or his estate or authorized representative) signing a separation agreement waiving any claims he may have arising out of his employment. The severance payments are inclusive of Dr. Lee's entitlement to payment for or in lieu of his 3 months' notice period. We may terminate Dr. Lee's employment without notice for Cause and Dr. Lee may terminate his employment without notice for Good Reason. In addition, if Dr. Lee is terminated due to his death, all his then unvested time-based shares would immediately accelerate and become fully exercisable. Dr. Lee is eligible for a shareholder value realization, or SVR, bonus, in which Dr. Lee, at the discretion of the remuneration committee, is eligible for a cash bonus in the event of a "Sale Event" (as defined in his employment agreement) on or before August 1, 2022. In the event of a "Sale Event" with proceeds of £450.0 million or less, Dr. Lee is entitled to a SVR bonus of 0.5% of the "Sales Event Proceeds" (as defined in his Employment Agreement). In the event of a "Sale Event" with proceeds between £450.0 million and £1.0 billion, Dr. Lee is entitled to a SVR bonus of 0.75% of the "Sales Event Proceeds". In the event of a "Sale Event" with proceeds of £1.0 billion or more, Dr. Lee is entitled to a SVR bonus of 1.0% of the "Sales Event Proceeds. For a description of Dr. Lee's current compensation, see "—Summary Compensation Table—2018".

Lee Kalowski, MBA. We will enter into an employment agreement with Mr. Kalowski, or the Kalowski Employment Agreement, which will be effective upon closing of this offering. Pursuant to the terms of the Kalowski Employment Agreement, Mr. Kalowski will continue to serve as our Chief Financial Officer and President. Mr. Kalowski will receive a salary of $450,000 which is subject to review and adjustment in accordance with our policy. Mr. Kalowski is eligible to receive an annual discretionary cash bonus of up to 40% of his base salary, subject to the terms of any applicable incentive compensation plan that may be in effect from time to time. Mr. Kalowski is eligible to participate in our employee benefit plans generally available to our executive employees, subject to the terms of those plans. Mr. Kalowski's employment has no specified term, but can be terminated at will by either party. Mr. Kalowski can be terminated with cause, at any time, pursuant to us providing him with written notice, in which event he would be entitled to certain accrued obligations. Mr. Kalowski can also be terminated without cause, or alternatively, Mr. Kalowski may terminate his employment with Good Reason, and (a) if such termination were to occur outside a change in control event, he would receive his base salary and other benefits including health insurance payments for nine months after his termination date along with other accrued benefits; and (b) if such termination were to occur inside a change in control event, he would receive his base salary and other benefits including health insurance payments for 12 months after his termination along with other accrued benefits, and his then unvested shares would immediately accelerate and become fully exercisable. In addition, if Mr. Kalowski is terminated due to his death or disability, all his then unvested time-based shares would immediately accelerate and become fully exercisable. The termination benefits would be contingent upon Mr. Kalowski (or his estate or authorized representative) signing a general release of claims upon his termination. For a description of Mr. Kalowski's current compensation, see "—Summary Compensation Table—2018".

Maria Koehler, M.D., Ph.D. Under an employment agreement that became effective on September 18, 2017, Dr. Koehler became our Chief Medical Officer. Dr. Koehler currently receives a salary of $385,500, which is subject to review and positive adjustment in accordance with our policy. Dr. Koehler was granted a sign-on award of $60,000, which must be repaid if Dr. Koehler leaves our company within 24 months of the effective date of her employment. Dr. Koehler is eligible to receive an annual discretionary cash bonus of up to 30% of her base salary, based on the achievement of certain performance goals, including corporate objectives, strategic initiatives and regulatory and clinical milestones, established by our board of directors. Dr. Koehler was also granted an option to purchase 107,519 ordinary shares, of which eighty percent (80%) vest over four years, and twenty percent (20%) of which vest on the earlier of: (i) four years from the date of the option grant or (ii) the date on which our board of directors determines that we have received income of $22.2 million in respect of our collaborations with AstraZeneca, Oxurion and collaboration partners. Dr. Koehler is eligible to participate in our employee benefit plans generally available to our executive employees, subject to the terms of those plans. Dr. Koehler's employment has no specified term, but may be terminated at will by us or Dr. Koehler. Dr. Koehler can be terminated with cause, at any time, pursuant to us providing her written notice, in which case she would be entitled to certain accrued obligations. Dr. Koehler can also be terminated without cause, and if so, she would receive her base salary and other benefits including health insurance payments for three months after her termination date along with other accrued obligations. The termination benefits would be contingent upon Dr. Koehler signing a general release of claims upon her termination. Dr. Koehler may terminate her employment with 60 days written notice and would then be entitled to certain accrued obligations. Dr. Koehler resigned from all positions with our company effective April 30, 2019.

Outstanding Equity Awards at Fiscal Year-End — 2018

The following table summarizes, for each of our named executive officers, the number of ordinary shares underlying outstanding share options and share awards held as of December 31, 2018.

	Option Awards[1]				
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)[3]	Option Expiration Date
Kevin Lee, Ph.D., MBA	12/17/2018[1]	—	164,743	$ 0.01	12/13/2029
Lee Kalowski, MBA	7/24/2017[2]	67,557	72,217	$ 1.49	7/23/2027
Maria Koehler, M.D., Ph.D.	9/18/2017[2]	48,384	59,135	$ 1.77	1/30/2028

(1) Commencing as of January 23, 2019, 7,974.3 of the shares subject to the option will vest every month through September 23, 2019; commencing as of October 23, 2019, 5,634.3 of the shares subject to the option will vest every month through March 23, 2020; commencing as of April 23, 2020, 4,509.7 of the shares subject to the option will vest every month through October 23, 2020; and commencing November 23, 2020, 3,947.5 of the shares subject to the option will vest every month through May 23, 2021, in each case provided that the named executive officer remains continuously employed with us through each applicable vesting date. The shares subject to the option are not early exercisable.

(2) 20% of the shares subject to the option will vest on the first anniversary of the grant date, 60% of the shares subject to the option will vest each month thereafter in 36 equal monthly installments, and the remaining 20% of the shares subject to the option will vest on the earlier of (i) the fourth anniversary of the grant date and (ii) the date in which our board of directors determines that we have received income of $22.2 million with respect to our collaborations with AstraZeneca, Oxurion, and any certain other collaborations, in all cases provided that the named executive officer remains continuously employed with us through each applicable vesting date.

(3) The amounts reported have been converted from GBP to USD using an exchange rate of $1.2763 to £1.00 as of December 31, 2018.

Equity Incentive Plans and Option Agreements

Option Agreements

On December 17, 2018, our board of directors approved the form of the unapproved bilateral option agreement for U.K. employees pursuant to which options to subscribe for ordinary shares can be granted to our employees and executive directors.

As of December 31, 2018, we have reserved 2,302,442 ordinary shares for the employee share option pool (amount to 16% of our issued share capital on a fully diluted basis) of which 744,196 ordinary shares have been issued, options for over 863,712 ordinary shares have been granted and 694,534 ordinary shares remain unallocated in the employee share option pool. Our board may act to increase the number of ordinary shares available for issuance.

In connection with certain corporate transactions, including a subdivision or consolidation or any other event that may affect the value of the options, the compensation committee has discretion to take action to prevent the dilution or enlargement of intended benefits, or to facilitate the transaction or event. In addition, in the event of a change in control, the compensation committee may accelerate the vesting and exercisability of any option in its discretion.

Our board of directors may amend the option agreement for future issuances of options at any time. However, no amendment may affect an award which has already been granted without the consent of the affected grantee.

2019 Share Option Plan

Our 2019 Plan was adopted by our board of directors on May 9, 2019 and approved by our shareholders on May 10, 2019 and will become effective upon the effectiveness of the registration statement of which this prospectus is part. The 2019 Plan will be utilized for all future share incentive awards following the closing of our initial public offering. The 2019 Plan allows the compensation committee to make equity-based and cash-based incentive awards to our officers, employees, directors and other key persons (including consultants). Except where the context indicates otherwise, references hereunder to our ordinary shares shall be deemed to include a number of ADSs equal to the number of ordinary shares.

We have initially reserved 2,470,583 ordinary shares, or the Initial Limit, for the issuance of awards under the 2019 Plan. The 2019 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase on the first day of each financial year, beginning on January 1, 2020, by 4% of the outstanding number of ordinary shares on the day prior to the first day of the applicable new financial year, or such lesser number of shares as determined by the Board, or the Annual Increase. This number is subject to adjustment in the event of a split-up, share dividend or other change in our capitalization.

The maximum aggregate number of shares that may be issued in the form of incentive share options shall not exceed the Initial Limit cumulatively increased the first day of each new financial year, starting on January 1, 2020 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 292,313 ordinary shares.

The 2019 Plan will be administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2019 Plan. Persons eligible to participate in the 2019 Plan will be those full or part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation committee in its discretion.

The 2019 Plan permits the granting of both options to subscribe for ordinary shares intended to qualify in relation to U.S. employees as incentive share options under Section 422 of the Code, and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our ordinary shares on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

The 2019 Plan provides that in the case of, and subject to, the consummation of a "change of control" as defined in the 2019 Plan, then (i) all unvested options shall lapse unless and to the extent the Compensation Committee determines otherwise; (ii) all vested options may be exercised on the same day as, and immediately prior to, the change of control becoming effective or within such period not exceeding six months afterwards as the Compensation Committee may determine, and any vested options not exercised within such period shall lapse.

Our board of directors may amend or discontinue the 2019 Plan and our compensation committee may amend the exercise price of options and amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose but no such action which would abrogate or adversely affect the subsisting rights of option holders unless it is made with either: (i) the written consent of the number of option holders who hold options to acquire for 75% of the ordinary shares which would be issued or transferred if all the subsisting options were exercised; or (ii) by a resolution of a meeting of option holders passed by not less than 75% of the option

holders who attend and vote either in person or proxy. Certain amendments to the 2019 Plan require the approval of our shareholders. No awards may be granted under the 2019 Plan after the date that is 10 years from the adoption date of the 2019 Plan. No awards under the 2019 Plan have been made prior to the date of this prospectus.

2019 Employee Share Purchase Plan

Our 2019 Employee Share Purchase Plan, or the ESPP, was adopted by our board of directors on May 9, 2019 and approved by our shareholders on May 10, 2019 and will become effective upon the effectiveness of the registration statement of which this prospectus is part. The ESPP is intended to qualify in relation to U.S. employees as an "employee share purchase plan" within the meaning of Section 423(b) of the Code. Except where the context indicates otherwise, references hereunder to our ordinary shares shall be deemed to include a number of ADSs equal to the number of ordinary shares. The ESPP initially reserves and authorizes the issuance of up to a total of 215,000 ordinary shares to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020 and each January 1 thereafter through January 1, 2029, by the least of (i) 1% of the outstanding number of ordinary shares on the immediately preceding December 31; (ii) 430,000 ordinary shares or (iii) such lesser number of shares as determined by the Compensation Committee. The number of shares reserved under the ESPP is subject to adjustment in the event of a split-up, share dividend or other change in our capitalization.

All employees who have completed at least three months of employment and whose customary employment is for more than 20 hours per week are eligible to participate in the ESPP.

We will make one or more offerings each year to our employees to purchase shares under the ESPP. Unless otherwise determined by our compensation committee, offerings will usually begin on the first business day occurring on or after June 1 and December 1 and will end on the last business day occurring on or before the following November 30 and May 31, referred to as offering periods. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 business days before the relevant offering date.

Each employee who is a participant in the ESPP may purchase shares by authorizing payroll deductions at a minimum of 1% up to a maximum of 15% of his or her base compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase shares on the last day of the offering period at a price equal to 85% of the fair market value of the shares on the first day or the last day of the offering period, whichever is lower. Under applicable U.S. tax rules, an employee may purchase no more than $25,000 worth of ordinary shares, valued at the start of the purchase period, under the ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the ESPP terminate upon the next business day following the employee's voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

The ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of ordinary shares authorized under the ESPP and certain other amendments require the approval of our shareholders.

Pension Plan

We currently maintain a personal pension plan provided by Scottish Widows Group where we make contributions to our U.K. eligible employee's personal pension plan as selected by the Company. Each participant may make additional contributions at his or her discretion.

401(k) Plan

We maintain a tax-qualified retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax-advantaged basis. Plan participants are able to defer eligible compensation subject to applicable annual Code limits. We have the ability to make discretionary contributions to the 401(k) plan and currently match each participant's contribution up to a maximum of 4% of their eligible compensation The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan's related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan.

Senior Executive Cash Incentive Bonus Plan

In May 2019, our board of directors adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or corporate performance goals, as well as individual performance objectives.

Our compensation committee may select corporate performance goals from among the following: achievement of cash flow (including, but not limited to, operating cash flow and free cash flow); research and development, publication, clinical and/or regulatory milestones; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our ADSs; economic value-added; acquisitions or strategic transactions, including licenses, collaborations, joint ventures or promotion arrangements; operating income (loss); return on capital, assets, equity, or investment; total shareholder returns; coverage decisions; productivity; expense efficiency; margins; operating efficiency; working capital; earnings (loss) per share of our ADSs; sales or market shares; number of prescriptions or prescribing physicians; revenue; corporate revenue; operating income and/or net annual recurring revenue, any of which may be (A) measured in absolute terms or compared to any incremental increase, (B) measured in terms of growth, (C) compared to another company or companies or to results of a peer group, (D) measured against the market as a whole and/or as compared to applicable market indices and/or (E) measured on a pre-tax or post-tax basis (if applicable).

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The corporate performance goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. Subject to the rights contained in any agreement between the executive officer and us, an executive officer must be employed by us on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion and provides the compensation committee with

discretion to adjust the size of the award as it deems appropriate to account for unforeseen factors beyond management's control that affected corporate performance.

Insurance and Indemnification

To the extent permitted by the Companies Act, we are empowered to indemnify our directors against any liability they incur by reason of their directorship. We maintain directors' and officers' insurance to insure such persons against certain liabilities. We expect to enter into a deed of indemnity with each of our directors and executive officers prior to the completion of this offering.

In addition to such indemnification, we provide our directors and executive officers with directors' and officers' liability insurance.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to our board of directors, executive officers, or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

NON-EMPLOYEE DIRECTOR COMPENSATION

Other than as set forth in the table and described more fully below, we did not pay any compensation or make any equity awards or non-equity awards to any of our non-employee directors during the year ended December 31, 2018. Directors may be reimbursed for travel and other expenses directly related to their activities as directors. Directors who also serve as employees receive no additional compensation for their service as directors. During the year ended December 31, 2018, Dr. Lee, our Chief Executive Officer, was a member of our board of directors, as well as an employee, and thus received no additional compensation for his services as a director. See the section titled "Executive Compensation" for more information about Dr. Lee's compensation for the year ended December 31, 2018. The following table presents the total compensation for each person who served as a non-employee director during the year ended December 31, 2018.

Name	Fees Earned or Paid in Cash ($)	Total ($)
Stephen Hoffman, M.D., Ph.D.[1]	9,000	9,000
Michael Anstey, DPhil[2]	—	—
Kate Bingham, MBA[2]	—	—
Deborah Harland, Ph.D., MBA[2]	—	—
Anja König, Ph.D.[2]	—	—
Eashwar Krishnan[2]	—	—
James Lee[2]	—	—
Carolyn Ng, Ph.D.[2]	—	—
Jason Rhodes, MBA[2]	—	—
Sir Greg Winter, FRS[2]	—	—

(1) As of December 31, 2018, Dr. Hoffman held restricted share awards for 80,638 ordinary shares. Dr. Hoffman departed from the board of directors on March 18, 2019.

(2) Each of Michael Anstey, Kate Bingham, Deborah Harland, Anja König, James Lee, Carolyn Ng, Jason Rhodes and Sir Greg Winter did not receive any compensation for the year ended December 31, 2018, and none of them held any outstanding equity awards as of December 31, 2018. James Lee resigned from the board of directors on July 12, 2018. Eashwar Krishnan joined the board of directors on December 22, 2018. Upon effectiveness of the registration statement of which this prospectus forms a part, Mr. Krishnan will resign as a member of our board of directors, and Bosun Hau will become a member of our board of directors.

In March 2019, Pierre Legault joined the board of directors as chairman. In his role as chairman, Mr. Legault will receive an annual fee of £5,000. In April 2019, Mr. Legault was also granted options to purchase 218,312 ordinary shares, which was equivalent to 1.5% of the equity in the company on the grant date, and which will be subject to anti-dilution protection until the earlier of (i) the completion of this offering or (ii) two years from March 15, 2019. For additional information, see "Certain Relationships and Related Party Transactions—Stone Sunny Isles, Inc."

Prior to this offering, we did not have a formal policy to compensate our non-employee directors. Immediately prior to the completion of this offering, we intend to implement a formal policy pursuant to which our non-employee directors will be eligible to receive the cash retainers

and equity awards discussed below: Mr. Legault will not participate in the cash retainer part of this policy and will instead continue to receive his annual retainer.

Annual Retainer for Board Membership	
Annual service on the board of directors (other than chair)	$ 40,000
Additional Annual Retainer for Committee Membership	
Annual service as member of the audit committee (other than chair)	$ 8,500
Annual service as chair of the audit committee	$ 17,000
Annual service as member of the compensation committee (other than chair)	$ 6,500
Annual service as chair of the compensation committee	$ 13,000
Annual service as member of the nominating and corporate governance committee (other than chair)	$ 4,000
Annual service as chair of the nominating and corporate governance committee	$ 8,000

Our policy will provide that, upon initial election to our board of directors, each non-employee director will be granted an equity award of 23,798 shares, or the Initial Grant. In addition, on the date of each of our annual meeting of shareholders following the completion of this offering, each non-employee director (other than the chair) who will continue as a non-employee director following such meeting will be granted an annual equity award of 11,899 shares and the chair will be granted 23,798 shares, or the Annual Grant. If a new non-employee director joins our board of directors on a date other than the date of our annual meeting of shareholders, such non-employee director will be granted a pro-rata portion of the Annual Grant, based on the time between his or her appointment and our next annual meeting of shareholders. The Initial Grant will vest in equal annual installments over three years, subject to continued service as a director through the applicable vesting dates. The Annual Grant will vest in full on the earlier of (i) the first anniversary of the grant date or (ii) our next annual meeting of shareholders, subject to continued service as a director through the applicable vesting date. Such awards are subject to full accelerated vesting upon the sale of our company.

Employee directors will receive no additional compensation for their service as a director.

We will reimburse all reasonable out-of-pocket expenses incurred by directors for their attendance at meetings of our board of directors or any committee thereof.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Within this section, we have calculated the dollar amounts using the historical exchange rate as of the closing date of each transaction. Other than compensation arrangements, we describe below transactions and series of similar transactions, since January 1, 2015, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000 or 1% of our total assets at year end for the last two completed fiscal years; and
- any of our directors, executive officers or holders of more than 5% of our share capital, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

Preferred Share Financings

Series A Financing

On October 6, 2014, we entered into a Series A Investment Agreement relating to BicycleRD Limited, pursuant to which we agreed to issue, and the subscribers agreed to subscribe for, up to 2,030,001 Series A convertible preferred shares at price of £10.00 per Series A preferred share in three tranches. We issued 811,998 Series A convertible preferred shares for an aggregate cash subscription price of $13.0 million on October 6, 2014. The Series A Investment Agreement provided for second and third closings based on the achievement of defined performance milestones. Subsequently, we and the subscribers (amongst others) amended the Series A Investment Agreement to increase the Series A convertible preferred shares issued in the second closing and reduce the Series A convertible preferred shares issued in the third closing. We issued 812,002 Series A convertible preferred shares for an aggregate cash subscription price of $11.5 million on March 11, 2016, and 406,001 Series A convertible preferred shares for an aggregate cash subscription price of $5.3 million on October 3, 2016.

The following table summarizes the participation in the Series A financing across all three tranches by any of our directors, executive officers, holders of more than 5% of our share capital, or any member of the immediate family of the foregoing persons.

Name	Series A Preferred Shares		Aggregate Purchase Price Paid
Sir Greg Winter[1]	30,000	£	300,000
Atlas Venture Fund VII LP[2]	451,299	£	4,512,990
Novartis Bioventures Ltd[2]	451,299	£	4,512,990
S.R. One, Limited	451,299	£	4,512,990
SVLS[3]	451,299	£	4,512,990

(1) Sir Greg Winter is a member of our board of directors.

(2) This entity holds, in the aggregate, more than 5% of our share capital.

(3) Consists of (i) 441,959 Series A convertible preferred shares held by SVLS Life Sciences Fund V, L.P. and (ii) 9,340 Series A convertible preferred shares held by SVLS Life Sciences Fund V Strategic Partners, L.P. These entities together hold, in the aggregate, more than 5% of our share capital.

On May 26, 2017, we issued warrants to subscribe for 200,000 Series A convertible preferred shares (or equivalent ordinary shares if exercised prior to the consummation of an initial public offering) to certain existing shareholders of BicycleRD Limited.

The following table summarizes the issuance of warrants to subscribe for Series A convertible preferred shares to any of our directors, executive officers, holders of more than 5% of our share capital, or any member of the immediate family of the foregoing persons.

Name	Series A Preferred Share Warrants	Aggregate Exercise Price
Atlas Venture Fund VIII LP[1]	50,000	£ 500
Novartis Bioventures Ltd[1]	50,000	£ 500
Sir Greg Winter[2]	50,000	£ 500

(1) This entity holds, in the aggregate, more than 5% of our share capital.

(2) Sir Greg Winter is a member of our board of directors.

Series B Financing

On May 26, 2017, we entered into a Series B Investment Agreement pursuant to which we agreed to issue, and the subscribers agreed to subscribe for 3,562,583 Series B convertible preferred shares (then called Series B convertible preferred shares) at a price per Series B1 convertible preferred share of £11.2278 in a single tranche for an aggregate cash subscription price of $51.9 million. In conjunction with the issue of the Series B1 convertible preferred shares, we also issued warrants to subscribe for up to 627,903 Series B1 convertible preferred shares to the subscribers of the Series B1 convertible preferred shares.

In addition, on October 27, 2017, we entered into an Amended and Restated Series B Investment Agreement relating to BicycleRD Limited, pursuant to which an unaffiliated investor subscribed for a further 384,615 Series B1 convertible preferred shares at a Series B1 convertible preferred shares per Series B1 convertible preferred shares of £13.00, in a single tranche for an aggregate cash subscription price of $6.6 million. In conjunction with this financing, we also issued warrants to subscribe for 115,384 Series B1 convertible preferred shares to the subscriber of the Series B1 convertible preferred shares.

The following table summarizes the participation in the Series B1 financing (on May 26, 2017 and October 27, 2017) by any of our directors, executive officers, holders of more than 5% of our share capital or any member of the immediate family of the foregoing persons.

Name	Series B1 Preferred Shares	Aggregate Purchase Price Paid
Atlas Venture Fund VIII LP[1]	133,596	£ 1,499,989
Novartis Bioventures Ltd[1]	445,323	£ 4,999,998
S.R. One, Limited[1]	445,323	£ 4,999,998
SVLS[2]	445,323	£ 4,999,998
Vertex Global Healthcare Fund I PTE. Ltd[1]	890,646	£ 9,999,995
Cambridge Innovation Capital (Jersey) Limited[1]	757,049	£ 8,499,995
Longwood Fund IV, L.P.[1]	445,323	£ 4,999,998
Ahren Innovation Capital Holding Limited[1]	384,615	£ 4,999,995

(1) This entity holds, in the aggregate, more than 5% of our share capital.

(2) Consists of (i) 436,107 Series B1 convertible preferred shares held by SVLS Life Sciences Fund V, L.P. and (ii) 9,216 Series B1 convertible preferred shares held by SV Life Sciences Fund V Strategic Partners, L.P. These entities together hold, in the aggregate, more than 5% of our share capital.

The following table summarizes the issuance of warrants to subscribe for Series B1 convertible preferred shares (or equivalent ordinary shares if exercised prior to the consummation of an initial public offering) to any of our directors, executive officers, holders of more than 5% of our share capital, or any member of the immediate family of the foregoing persons.

Name	Series B1 Preferred Share Warrants	Aggregate Exercise Price
Vertex Global Healthcare Fund I PTE. Ltd(1)	267,193	£ 2,672
Cambridge Innovation Capital (Jersey) Limited(1)	227,114	£ 2,271
Longwood Fund IV, L.P.(1)	133,596	£ 1,336
Ahren Innovation Capital Holding Limited(1)	115,384	£ 1,154

(1) This entity holds, in the aggregate, more than 5% of our share capital.

Series B2 Financing

In December 2018, we entered into an investment agreement relating to Bicycle Therapeutics Limited pursuant to which we agreed to issue, and the subscribers agreed to subscribe for 1,403,633 Series B2 convertible preferred shares at a price per Series B2 preferred share of £15.55, for an aggregate cash subscription price of $27.9 million. In December 2018 (and in conjunction with the Series B2 financing), the existing holders of warrants to subscribe for Series B1 convertible preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 convertible preferred shares (or equivalent ordinary shares if exercised prior to the consummation of an initial public offering) in the proportions set out below and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 convertible preferred shares (or equivalent ordinary shares if exercised prior to the consummation of an initial public offering) to Aquila Investments IV, an entity affiliated with Tybourne Capital Management (HK) Limited, at an aggregate exercise price of £1,949.

Name	No. of Series B1 Warrants Surrendered
Vertex Global HC Fund I Pte. Ltd.(1)	68,918
Cambridge Innovation Capital (Jersey) Limited(1)	51,345
Longwood Fund IV, LP(1)	48,314
Entities associated with Ahren Innovation Capital Holding Limited(1)	26,334

(1) This entity holds or will hold, after giving effect to the Series B2 financing, in the aggregate, more than 5% of our share capital.

The following table summarizes the participation in the Series B2 financing by any of our directors, executive officers, holders of more than 5% of our share capital, or any member of the immediate family of the foregoing persons.

Name	Series B2 Preferred Shares	Aggregate Purchase Price Paid
An entity affiliated with Tybourne Capital Management (HK) Limited[1]	1,017,783	£15,826,526
Cambridge Innovation Capital (Jersey) Limited[1]	160,771	£2,499,989
Vertex Global Healthcare Fund I PTE. Ltd[1]	144,694	£2,249,992
Entities associated with Ahren Innovation Capital Holdings Limited[1]	80,385	£1,249,987

(1) This entity holds or will hold, after giving effect to the Series B2 financing, in the aggregate, more than 5% of our share capital.

Consulting Agreement with Stone Sunny Isles, Inc.

In March 2019, we entered into a consultancy agreement with Stone Sunny Isles, Inc., or Stone Sunny Isles, pursuant to which Stone Sunny Isles has agreed to make available Pierre Legault to provide advisory services to us as requested by our board of directors or our chief executive officer. In consideration for the provision of the advisory services, we pay Stone Sunny Isles a monthly retainer of £10,416, which is billed in U.S. Dollars. Pierre Legault is the President, Treasurer and Director of Stone Sunny Isles.

Consulting Agreement with 10X Capital, Inc.

In April 2016, we entered into a consulting agreement with 10X Capital, Inc., or 10X Capital, pursuant to which 10X Capital agreed to make available Stephen Hoffman to provide advisory services to us as requested by the board of directors or by our chief executive officer. In consideration for the provision of the advisory services, we paid 10X Capital a monthly fee of $8,250. We have served notice to terminate this agreement in accordance with its terms in conjunction with Mr. Hoffman's departure from the board of directors in March 2019.

Founder Royalty Arrangements

We have entered into two royalty agreements with our founders, Christian Heinis, John Tite, and Sir Greg Winter, and our initial investors, Atlas Venture Fund VIII LP, Novartis Bioventures LTD. Pursuant to the first royalty agreement, we are obligated to pay a royalty percentage in the low single digits on net sales arising from products licensed under the Oxurion collaboration agreement. Pursuant to the second royalty agreement, we are obligated to pay a royalty percentage in the low single digits on net sales arising from products licensed under the AstraZeneca collaboration agreement.

Agreements with Our Executive Officers and Directors

We have entered into employment agreements with certain of our executive officers and service agreements with our non-executive directors. These agreements contain customary provisions and representations, including confidentiality, non-competition, non-solicitation and inventions assignment undertakings by the executive officers. However, the enforceability of the non-competition provisions may be limited under applicable law.

Participation in this Offering

Certain of our existing shareholders and their affiliated entities, including those affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $25.0 million of ADSs in this offering at the initial public offering price per ADS and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no ADSs to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no ADSs in this offering.

Indemnification Agreements

We intend to enter into a deed of indemnity with each of our directors and executive officers prior to the completion of this offering. These agreements and our articles of association to be effective upon the completion of this offering require us to indemnify our directors and executive officers to the fullest extent permitted by law.

In addition, we have previously entered into and intend to enter into new agreements to indemnify our directors and executive officers. These agreements will, among other things, indemnify our directors and executive officers against certain liabilities and expenses incurred by such persons in connection with claims made by reason of their being such a director or executive officer.

Agreements With Our Shareholders

In connection with the preferred share financings, we entered into subscription and shareholder agreements containing registration rights and information rights, among other things, with certain holders of our convertible preferred shares. These shareholder agreements will terminate upon the closing of this offering, except for the registration rights granted under our investors' rights agreement, as more fully described in "Description of Share Capital and Articles of Association—Registration Rights."

Related Person Transaction Policy

In connection with this offering, we have adopted a written related party transactions policy that such transactions must be approved by our audit committee. This policy will become effective on the date on which the registration statement of which this prospectus is part is declared effective by the SEC. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving "related person transactions," which are transactions between us and related persons in which the related person has a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of any class of our voting securities, and their immediate family members.

PRINCIPAL SHAREHOLDERS

The following table sets forth certain information known to us regarding beneficial ownership of our share capital as of May 1, 2019 by:

- each person, or group of affiliated persons, known by us to be the beneficial owner of more than 5% of our voting securities;
- each of our named executive officers and other executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Except as noted by footnote, and subject to community property laws where applicable, we believe based on the information provided to us that the persons and entities named in the table below have sole voting and investment power with respect to all securities shown as beneficially owned by them. The information is not necessarily indicative of beneficial ownership for any other purpose.

Beneficial ownership is determined in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include ordinary shares that can be acquired within 60 days of May 1, 2019. Ordinary shares underlying convertible securities that can be acquired within 60 days of May 1, 2019 are deemed to be beneficially owned by the persons holding these securities for the purpose of computing percentage ownership of that person, but are not treated as outstanding for the purpose of computing any other person's ownership percentage.

Percentage ownership calculations are based on 912,977 shares (which includes 53,957 of unvested restricted shares subject to repurchase by us) outstanding as of May 1, 2019, and gives effect to (i) the exercise of warrants to subscribe for 200,000 Series A convertible preferred shares immediately prior to the completion of this offering, (ii) the exercise of warrants to subscribe for 371,645 Series B1 convertible preferred shares, and (iii) the automatic conversion of all outstanding convertible preferred shares as of May 1, 2019 into an aggregate of 12,464,406 ordinary shares, upon the completion of this offering. The percentage of shares beneficially owned after completion of this offering is based on 17,696,417 ordinary shares after this offering, including 4,333,333 ordinary shares in the form of ADSs issued in connection with this offering.

Certain of our existing shareholders and their affiliated entities, including those affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $25.0 million of ADSs in this offering at the initial public offering price per ADS and on the same terms as the other purchasers in this offering. The table below does reflect any potential purchases by such shareholders in this offering.

Except as otherwise indicated in the table below, addresses of the directors, executive officers and named beneficial owners are care of Bicycle Therapeutics Limited, Building 900 Babraham Research Campus, Babraham, Cambridge CB22 3AT, United Kingdom.

Name and Address of Beneficial Owner	Number of Ordinary Shares Beneficially Owned Prior to this Offering	Percentage of Ordinary Shares Beneficially Owned	
		Prior to this Offering	After this Offering
5% or Greater Shareholders			
Atlas Venture Fund VIII LP[1]	1,155,553	9.15%	6.52%
Novartis Bioventures Ltd[2]	1,601,011	12.67%	9.04%
S.R. One, Limited[3]	1,529,561	12.18%	8.64%
Entities affiliated with SVLS[4]	1,529,559	12.18%	8.64%
Vertex Global Healthcare Fund I PTE. Ltd[5]	1,621,168	12.76%	9.15%
Cambridge Innovation Capital (Jersey) Limited[6]	1,437,151	11.33%	8.11%
Longwood Fund IV, L.P.[7]	697,299	5.52%	3.94%
Entities affiliated with Ahren Innovation Capital Holding Limited[8]	728,108	5.77%	4.11%
An entity affiliated with Tybourne Capital Management (HK) Limited[9]	1,593,675	12.55%	9.00%
Directors, Named Executive Officers and Other Executive Officers			
Kevin Lee, Ph.D., MBA[10]	306,983	2.44%	1.73%
Lee Kalowski, MBA[11]	76,876	*%	*%
Peter Leone, MBA	—	*%	*%
Michael Skynner, Ph.D.[12]	48,589	*%	*%
Maria Koehler, M.D., Ph.D.[13]	55,549	*%	*%
Nick Keen, Ph.D.[14]	82,852	*%	*%
Pierre Legault, MBA, CPA[15]	6,064	*%	*%
Michael Anstey, DPhil[16]	1,437,151	11.33%	8.11%
Kate Bingham, MBA[17]	1,529,559	12.18%	8.64%
Deborah Harland, Ph.D., MBA[18]	1,529,561	12.18%	8.64%
Eashwar Krishnan[19]	1,593,675	12.55%	9.00%
Anja König, Ph.D.[20]	1,601,011	12.67%	9.04%
Carolyn Ng, Ph.D.[21]	1,621,168	12.76%	9.15%
Jason Rhodes, MBA[22]	1,155,553	9.15%	6.52%
Sir Greg Winter, FRS[23]	163,927	1.30%	*%
Director Nominee			
Bosun Hau, MBA[19]	—	—	—
All Directors, Executive Officers and Director Nominee as a Group (16 people)	11,208,520	88.69%	63.28%

* Represents beneficial ownership of less than one percent.

(1) Consists of 625,049 Series A Preferred Shares, 50,000 Series A Preferred Share Warrants and 133,596 Series B1 Preferred Shares. Jason Rhodes, MBA is a partner at Atlas Venture LP and is a member of our board of directors. The address of Atlas Venture Fund VIII LP is 400 Technology Square, Cambridge, MA 02139.

(2) Consists of 625,049 Series A Preferred Shares, 50,000 Series A Preferred Share Warrants and 445,323 Series B1 Preferred Shares. Anja König, Ph.D. is the global head of Novartis Venture Fund and is a member of our board of directors. The address of Novartis Bioventures Ltd is Lichtstrasse 35, 4056 Basel, Switzerland.

(3) Consists of 625,049 Series A Preferred Shares and 445,323 Series B1 Preferred Shares. Deborah Harland, Ph.D., MBA is a partner at S.R. One, Limited and is a member of our board of directors. The address of S.R. One, Limited is 161 Washington Street, Conshohocken, PA 19428.

(4) Consists of (i) 612,113 Series A Preferred Shares and 436,107 Series B1 Preferred Shares held by SVLS Life Sciences V, L.P. and (ii) 12,936 Series A Preferred Shares and 9,216 Series B1 Preferred Shares held by Kate Bingham, MBA is a managing partner of SV Health Managers LLP and a member of our board of directors. The address for both SVLS Life Sciences V, L.P. and SVLS Life Sciences Fund V Strategic Partners, L.P. is One Boston Place, Boston, MA 02108.

(5) Consists of 1,035,340 Series B1 Preferred Shares and 99,138 Series B1 Preferred Share Warrants. Carolyn Ng, Ph.D. is a principal of Vertex Ventures HC and a member of our board of directors. The address of Vertex Global Healthcare Fund I PTE. Ltd is 250 North Bridge Road, #11-01 Raffles City Tower, Singapore 179101.

(6) Consists of 917,820 Series B1 Preferred Shares and 87,885 Series B1 Preferred Share Warrants. Michael Anstey, DPhil is an investment director at Cambridge Innovation Captial plc and a member of our board of directors. The address of Cambridge Innovation Capital (Jersey) Limited is Gaspe House, 66-72 Esplanade, St. Helier, Jersey, Channel Islands, JE2 3QT.

(7) Consists of 445,323 Series B1 Preferred Shares and 42,641 Series B1 Preferred Share Warrants. The address of Longwood Fund IV, L.P. is 800 Bolyston, Boston, Massachusetts, 02199, USA.

(8) Consists of (i) 260,671 Series B1 Preferred Shares, 30,176 Series B1 Preferred Share Warrants and 80,385 Series B2 Preferred Shares held by Ahren LP, (ii) 113,366 Series B1 Preferred Shares and 13,124 Series B1 Preferred Share Warrants held by BAIV LP and (iii) 10,578 Series B1 Shares and 1,250 Series B1 Preferred Share Warrants held by SAIV LP. The address for Ahren LP, BAIV LP and SAIV LP is 15 Queens Grove, London, United Kingdom, NW8 6EL.

(9) Consists of 1,017,783 Series B1 Preferred Shares and 97,456 Series B1 Preferred Share Warrants held by Aquila Investments IV, an affiliate of Tybourne Capital Management. Eashwar Krishnan is the managing partner of Tybourne Capital Management and is a member of our board of directors. Upon effectiveness of the registration statement of which this prospectus forms a part, Mr. Krishnan will resign as a member of our board of directors, and Bosun Hau will become a member of our board of directors. Mr. Hau is the Managing Director and Co-Head of Private Equity at Tybourne Capital Management. The address of Tybourne Capital Management is 30/F, AIA Central, 1 Connaught Road Central, Hong Kong.

(10) Consists of 306,983 options to purchase ordinary shares exercisable within 60 days of May 1, 2019.

(11) Consists of 76,876 options to purchase ordinary shares exercisable within 60 days of May 1, 2019.

(12) Consists of 48,585 options to purchase ordinary shares exercisable within 60 days of May 1, 2019.

(13) Consists of 55,549 options to purchase ordinary shares exercisable within 60 days of May 1, 2019.

(14) Consists of 82,852 options to purchase ordinary shares exercisable within 60 days of May 1, 2019.

(15) Consists of 6,064 options to purchase ordinary shares exercisable within 60 days of May 1, 2019.

(16) Consists of 917,820 Series B1 Preferred Shares and 87,885 Series B1 Preferred Share Warrants.

(17) Consists of 625,049 Series A Preferred Shares and 445,323 Series B1 Preferred Shares.

(18) Consists of 625,049 Series A Preferred Shares and 445,323 Series B1 Preferred Shares.

(19) Consists of 1,017,783 Series B1 Preferred Shares and 97,456 Series B1 Preferred Share Warrants.

(20) Consists of 625,049 Series A Preferred Shares, 50,000 Series A Preferred Share Warrants and 445,323 Series B1 Preferred Shares.

(21) Consists of 1,035,340 Series B1 Preferred Shares and 99,138 Series B1 Preferred Share Warrants.

(22) Consists of 625,049 Series A Preferred Shares, 50,000 Series A Preferred Share Warrants and 133,596 Series B1 Preferred Shares.

(23) Consists of 30,000 Series A Preferred Shares, 20,187 options to purchase ordinary shares, 29,420 ordinary shares and 50,000 Series A Preferred Share Warrants.

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

The following describes our issued share capital, summarizes the material provisions of our articles of association and highlights certain differences in corporate law in the United Kingdom and the United States. Please note that this summary is not intended to be exhaustive. For further information, please refer to the full version of our articles of association, which are included as an exhibit to the registration statement of which this prospectus is a part.

We were incorporated pursuant to the laws of England and Wales as Bicycle Therapeutics Limited on October 27, 2017. We are registered with the Registrar of Companies in England and Wales under number 11036004, and our registered office is at Building 900 Babraham Research Campus, Babraham, Cambridge CB22 3AT, United Kingdom.

Certain resolutions have been passed by our shareholders in anticipation of the completion of this offering:

(a) the sum of £2,740.65 (being part of the share premium account) shall be capitalised and appropriate as capital to the holders of Ordinary Shares and the specific authorisation of our directors for the purposes of section 551 of the Companies Act 2006 to issue ordinary shares as bonus shares to the holders of Ordinary Shares up to a nominal amount of £2,740.65 for a period of five years;

(b) approval of the 2019 Share Option Plan and authorization of our directors for purposes of Section 551 of the Companies Act 2006 to issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £21,650.00 under the 2019 Share Option Plan for a period of five years;

(c) authorization of our directors for purposes of Section 551 of the Companies Act 2006 to issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £12,382.68 in respect to all the options issued under the existing plan prior to the offering for a period of five years;

(d) approval of the Employee Share Purchase Plan and authorization of our directors for purposes of Section 551 of the Companies Act 2006 to issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £2,150.00 under the Employee Share Purchase Plan for a period of five years;

(e) subject to and conditional upon the completion of the IPO (but effective immediately prior to the IPO), the conversion of the Preferred Shares, consisting of: (i) the re-designation of all the Preferred Shares into Ordinary Shares; and (ii) the sum of £34,966.97 (being part of the share premium account) shall be capitalised and appropriate as capital to the holders of Preferred Shares and that the Directors be authorise to apply such sum in paying up in full Ordinary Shares;

(f) the sum of £2,452.32 (being part of the share premium account) shall be capitalised and appropriate as capital to the holders of the Warrants and the specific authorisation of our directors for the purposes of section 551 of the Companies Act 2006 to issue ordinary shares as bonus shares to the holders of warrants up to a nominal amount of £8,168.77 for a period of five years;

(g) general authorization of our directors for purposes of Section 551 of the Companies Act 2006 to issue shares in the company and grant rights to subscribe for or convert any

securities into shares in the company up to a maximum aggregate nominal amount of £150,000.00 for a period of five years;

(h) empowering of our directors pursuant to Section 570 of Companies Act 2006 to issue equity securities for cash pursuant to the Section 551 authorities referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act 2006 did not apply to such allotments;

(i) the amount outstanding to the credit of the share premium account of the Company be reduced by £21,304,875.58 and the amount by which the share premium account is so reduced be credited to the Company's distributable reserves; and

(j) the adoption of new articles of association that will become effective upon the completion of this offering. See "—Post-IPO articles of association" below.

Certain further resolutions will be required to be passed by our shareholders prior to completion of this offering. These will include resolutions for the the Company be re-registered as a public limited liability company by the name of Bicycle Therapeutics plc, in accordance with section 90 of the Act.

Issued Share Capital

As of March 31, 2019, the issued share capital of Bicycle Therapeutics Limited was 898,678 ordinary shares which includes 56,643 of unvested restricted shares subject to repurchase, 2,800,001 Series A convertible preferred shares, 3,947,198 Series B1 convertible preferred shares and 1,403,633 Series B2 convertible preferred shares. The nominal value of our ordinary shares, Series A convertible preferred shares, Series B1 convertible preferred shares and Series B2 convertible preferred shares is £0.01 per share and each issued ordinary share, Series A convertible preferred share, Series B1 convertible preferred share and Series B2 convertible preferred share is fully paid (or deemed paid up).

Ordinary Shares

In accordance with our articles of association to be in effect upon the completion of this offering, the following summarizes the rights of holders of our ordinary shares:

- each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;
- the holders of the ordinary shares shall be entitled to receive notice of, attend, speak and vote at our general meetings; and
- holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

We are required by the Companies Act to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar.

Holders of our ADSs will not be treated as one of our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will

be the holder of the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see "Description of American Depositary Shares" in this prospectus.

Under the Companies Act, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in this offering, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of this offering. We also are required by the Companies Act to register a transfer of shares (or give the transferee notice of and reasons for refusal as the transferee may reasonably request) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

- the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or
- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such delay does not prevent dealings in the shares taking place on an open and proper basis.

Preemptive Rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). On May 10, 2019, our shareholders approved the exclusion of preemptive rights for a period of five years from the date of approval, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period). On May 10, 2019, our shareholders approved the exclusion of preemptive rights for the allotment of ordinary shares in connection with this offering.

Distributions and Dividends

Under the Companies Act, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves, as determined on a non-consolidated basis. The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under English law.

Once we are a public company, it will not be sufficient that we have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement will be

imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

- if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and
- if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of its net assets to less than that total.

Disclosure of Interest in Shares

Pursuant to Part 22 of the Companies Act, a company is empowered by notice in writing to require any person whom the company knows to be, or has reasonable cause to believe to be, interested in the company's shares or at any time during the three years immediately preceding the date on which the notice is issued to have been so interested, within a reasonable time to disclose to the company details of that person's interest and (so far as is within such person's knowledge) details of any other interest that subsists or subsisted in those shares.

If a shareholder defaults in supplying the company with the required details in relation to the shares in question, or the Default Shares, the shareholder shall not be entitled to vote or exercise any other right conferred by membership in relation to general meetings. Where the Default Shares represent 0.25% or more of the issued shares of the class in question, the directors may direct that:

- any dividend or other money payable in respect of the Default Shares shall be retained by the company without any liability to pay interest on it when such dividend or other money is finally paid to the shareholder; and/or
- no transfer by the relevant shareholder of shares (other than a transfer approved in accordance with the provisions of the company's articles of association) may be registered (unless such shareholder is not in default and the transfer does not relate to default shares).

Purchase of Own Shares

English law permits a public limited company to purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, subject to complying with procedural requirements under the Companies Act and provided that its articles of association do not prohibit it from doing so. Our articles of association, a summary of which is provided above, do not prohibit us from purchasing our own shares. A public limited company must not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares.

Any such purchase will be either a "market purchase" or "off market purchase," each as defined in the Companies Act. A "market purchase" is a purchase made on a "recognized investment exchange (other than an overseas exchange) as defined in the UK Financial Services and Markets Act 2000, or FSMA. An "off market purchase" is a purchase that is not made on a "recognized investment exchange." Both "market purchases" and "off market purchases" require prior shareholder approval by way of an ordinary resolution. In the case of an "off market purchase," a company's shareholders, other than the shareholders from whom the company is purchasing shares, must approve the terms of the contract to purchase shares and in the case of a "market purchase," the shareholders must approve the maximum number of shares that can be purchased and the maximum and minimum prices to be paid by the company.

Nasdaq is an "overseas exchange" for the purposes of the Companies Act and does not fall within the definition of a "recognized investment exchange" for the purposes of FSMA and any purchase made by us would need to comply with the procedural requirements under the Companies Act that regulate "off market purchases."

A share buy back by a company of its shares will give rise to U.K. stamp duty reserve tax and stamp duty at the rate of 0.5% of the amount or value of the consideration payable by the company (rounded up to the next £5.00), and such stamp duty reserve tax or duty will be paid by the company. The charge to stamp duty reserve tax will be canceled or, if already paid, repaid (generally with interest), where a transfer instrument for stamp duty purposes has been duly stamped within six years of the charge arising (either by paying the stamp duty or by claiming an appropriate relief) or if the instrument is otherwise exempt from stamp duty.

Our articles of association do not have conditions governing changes to our capital which are more stringent that those required by law.

Shareholder Rights

Certain rights granted under the Companies Act, including the right to requisition a general meeting or require a resolution to be put to shareholders at the annual general meeting, are only available to our members. For English law purposes, our members are the persons who are registered as the owners of the legal title to the shares and whose names are recorded in our register of members. In the case of shares held in a settlement system operated by the Depository Trust Company, or DTC, the registered member will be DTC's nominee, Cede & Co. If a person who holds their ADSs in DTC wishes to exercise certain of the rights granted under the Companies Act, they may be required to first take steps to withdraw their ADSs from the settlement system operated by DTC and become the registered holder of the shares in our register of members. A withdrawal of shares from DTC may have tax implications, for additional information on the potential tax implications of withdrawing your shares from the settlement system operated by DTC, see "Material Tax Considerations—United Kingdom Taxation."

Registration Rights

Upon the completion of this offering, the holders of 12,464,406 shares of our ordinary shares issuable upon the conversion of our convertible preferred shares plus the ordinary shares issued as bonus shares to holders of convertible preferred shares and the ordinary shares issued on exercise of the warrants held by the holders of convertible preferred shares, will be entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of a registration rights agreement between us and holders of the holders of the convertible preferred shares. The registration rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights.

Demand Registration Rights

Beginning 180 days after the effective date of the registration statement of which this prospectus forms a part, the holders of 12,464,406 shares of our ordinary shares issuable upon the conversion of convertible preferred shares upon closing of this offering are entitled to demand registration rights. Under the terms of the registration rights agreement, we will be required, upon the written request of holders of a majority of these securities to file a registration statement and use best efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the investment and shareholders' agreement.

Short-Form Registration Rights

Pursuant to the registration rights agreement, if we are eligible to file a registration statement on Form F-3 or Form S-3, upon the written request a holder of securities at an aggregate offer price of at least $10 million, we will be required to effect a registration of such shares. We are required to effect only two registrations in any twelve month period pursuant to this provision of the registration rights agreement. The right to have such shares registered on Form F-3 or Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the registration rights agreement, if we register any of our securities either for our own account or for the account of other security holders, other than in connection with our initial public offering or a registration for any employee benefit plan, corporate reorganization, or the offer or sale of debt securities, the holders of the relevant shares (for so long as they are a party to the registration rights agreement) are entitled to include their shares in the registration. Subject to certain exceptions contained in the registration rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our registration rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The registration rights granted under the registration rights agreement will terminate on the earliest of (i) in respect of any holder, at such time as the holder holds less than 1% of the Company's outstanding ordinary shares; (ii) the three anniversary of the completion of this offering and (iii) such time as the Company has completion the offering and all relevant ordinary shares may be sold pursuant to rule 144 during a 90 day period without registration.

Post-IPO Articles of Association

Our Articles of Association, or the Articles, were approved by our shareholders in May 2019 and were adopted with effect from the completion of the offering. A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles.

The Articles contain no specific restrictions on our purpose and therefore, by virtue of section 31(1) of the Companies Act, our purpose is unrestricted.

The Articles contain, among other things, provisions to the following effect:

Share Capital

Our share capital will consist of ordinary shares. We may issue shares with such rights or restrictions as may be determined by ordinary resolution, including shares which are to be redeemed, or are liable to be redeemed at our option or the holder of such shares.

Voting

The shareholders have the right to receive notice of, and to vote at, our general meetings. Each shareholder who is present in person (or, being a corporation, by representative) at a general meeting on a show of hands has one vote and, on a poll, every such holder who is present in person (or, being a corporation, by representative) or by proxy has one vote in respect of every share held by him.

Variation of Rights

Whenever our share capital is divided into different classes of shares, the special rights attached to any class may be varied or abrogated either with the consent in writing of the holders of three-fourths in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class and may be so varied and abrogated whilst the company is a going concern.

Dividends

We may, subject to the provisions of the Companies Act and the Articles, by ordinary resolution from time to time declare dividends to be paid to shareholders not exceeding the amount recommended by our board of directors. Subject to the provisions of the Companies Act, in so far as, in the board of directors' opinions, our profits justify such payments, the board of directors may pay interim dividends on any class of our shares.

Any dividend unclaimed after a period of 12 years from the date such dividend was declared or became payable shall, if the board of directors resolve, be forfeited and shall revert to us. No dividend or other moneys payable on or in respect of a share shall bear interest as against us.

Liquidation Preference

On a distribution of assets on a liquidation, the surplus assets remaining after payment of liabilities shall be distributed among the holders of ordinary shares pro rata to the number of ordinary shares held.

Transfer of Ordinary Shares

Each member may transfer all or any of his shares which are in certificated form by means of an instrument of transfer in any usual form or in any other form which the board of directors may approve. Each member may transfer all or any of his shares which are in uncertificated form by means of a "relevant system" (i.e., the CREST System) in such manner provided for, and subject as provided in, the CREST Regulations.

The Board may, in its absolute discretion, refuse to register a transfer of certificated shares unless:

(i) it is for a share which is fully paid up;

(ii) it is for a share upon which the company has no lien;

(iii) it is only for one class of share;

(iv) it is in favor of a single transferee or no more than four joint transferees;

(v) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the board of directors to be exempt from stamp duty; and

(vi) it is delivered for registration to the registered office of the company (or such other place as the board of directors may determine), accompanied (except in the case of a transfer by a person to whom the company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the board of directors may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

The board of directors may refuse to register a transfer of uncertificated shares in any circumstances that are allowed or required by the CREST Regulations and the CREST System.

Allotment of Shares and Preemption Rights

Subject to the Companies Act and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the company may by ordinary resolution determine, or if no ordinary resolution has been passed or so far as the resolution does not make specific provision, as the board of directors may determine (including shares which are to be redeemed, or are liable to be redeemed at the option of the company or the holder of such shares).

In accordance with section 551 of the Companies Act, the board of directors may be generally and unconditionally authorized to exercise all the powers of the company to allot shares up to an aggregate nominal amount equal to the amount stated in the relevant ordinary resolution authorizing such allotment. The authorities passed on May 13, 2019 and remains in force at the date of this prospectus.

The provisions of section 561 of the Companies Act (which confer on shareholders rights of preemption in respect of the allotment of equity securities which are paid up in cash) apply to the company except to the extent disapplied by special resolution of the company. Such preemption rights have been disapplied pursuant to the special resolution passed on May 13, 2019.

Alteration of Share Capital

The company may by ordinary resolution consolidate or divide all of its share capital into shares of larger nominal value than its existing shares, or cancel any shares which, at the date of the ordinary resolution, have not been taken or agreed to be taken by any person and diminish the amount of its share capital by the nominal amount of shares so cancelled or sub-divide its shares, or any of them, into shares of smaller nominal value.

The company may, in accordance with the Companies Act, reduce or cancel its share capital or any capital redemption reserve or share premium account in any manner and with and subject to any conditions, authorities and consents required by law.

Board of Directors

Unless otherwise determined by the company by ordinary resolution, the number of directors (other than any alternate directors) shall not be less than two, but there shall be no maximum number of directors.

Subject to the Articles and the Companies Act, the company may by ordinary resolution appoint a person who is willing to act as a director and the board of directors shall have power at any time to appoint any person who is willing to act as a director, in both cases either to fill a vacancy or as an addition to the existing board of directors.

The Articles of Association provide that upon completion of this offering, our board of directors will be divided into three classes, each of which will consist, as nearly as possible, of one-third of the total number of directors constituting our entire board and which will serve staggered three-year terms. At each annual general meeting, the successors of directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election.

At every subsequent annual general meeting any director who either (i) has been appointed by the board of directors since the last annual general meeting or (ii) was not appointed or reappointed at one of the preceding two annual general meetings, must retire from office and may offer themselves for reappointment by the shareholders by ordinary resolution.

Subject to the provisions of the Articles, the board of directors may regulate their proceedings as they deem appropriate. A director may, and the secretary at the request of a director shall, call a meeting of the directors.

The quorum for a meeting of the board of directors shall be fixed from time to time by a decision of the board of directors, but it must never be less than two and unless otherwise fixed, it is two.

Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director having one vote. In the case of an equality of votes, the chairman will only have a casting vote or second vote when an acquisition has been completed.

Directors shall be entitled to receive such remuneration as the board shall determine for their services to the company as directors, and for any other service which they undertake for the company provided that the aggregate fees payable to the directors must not exceed £ per annum. The directors shall also be entitled to be paid all reasonable expenses properly incurred by them in connection with their attendance at meetings of shareholders or class meetings, board of director or committee meetings or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the company.

The board of directors may, in accordance with the requirements in the Articles, authorize any matter proposed to them by any director which would, if not authorized, involve a director breaching his duty under the Companies Act, to avoid conflicts of interests.

A director seeking authorization in respect of such conflict shall declare to the board of directors the nature and extent of his interest in a conflict as soon as is reasonably practicable. The director shall provide the board with such details of the matter as are necessary for the board to decide how to address the conflict together with such additional information as may be requested by the board.

Any authorization by the board of directors will be effective only if:

(i) to the extent permitted by the Companies Act, the matter in question shall have been proposed by any director for consideration in the same way that any other matter may be proposed to the directors under the provisions of the Articles;

(ii) any requirement as to the quorum for consideration of the relevant matter is met without counting the conflicted director and any other conflicted director; and

(iii) the matter is agreed to without the conflicted director voting or would be agreed to if the conflicted director's and any other interested director's vote is not counted.

Subject to the provisions of the Companies Act, every director, secretary or other officer of the company (other than an auditor) is entitled to be indemnified against all costs, charges, losses,

damages and liabilities incurred by him in the actual purported exercise or discharge of his duties or exercise of his powers or otherwise in relation to them.

General Meetings

The company must convene and hold general meetings in accordance with the Companies Act. Under the Companies Act, an annual general meeting must be called by notice of at least 21 days and a general meeting must be called by notice of at least 14 days.

No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business, but the absence of a quorum shall not preclude the choice or appointment of a chairman of the meeting which shall not be treated as part of the business of the meeting. Save as otherwise provided by the Articles, two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

Borrowing Powers

Subject to the Articles and the Companies Act, the board of directors may exercise all of the powers of the company to:

(a) borrow money;

(b) indemnify and guarantee;

(c) mortgage or charge;

(d) create and issue debentures and other securities; and

(e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

Capitalization of Profits

The directors may, if they are so authorized by an ordinary resolution of the shareholders, decide to capitalize any undivided profits of the company (whether or not they are available for distribution), or any sum standing to the credit of the company's share premium account or capital redemption reserve. The directors may also, subject to the aforementioned ordinary resolution, appropriate any sum which they so decide to capitalize to the persons who would have been entitled to it if it were distributed by way of dividend and in the same proportions.

Limitation on Owning Securities

Our articles of association do not restrict in any way the ownership or voting of our shares by non-residents.

Uncertificated Shares

Subject to the Companies Act, the board of directors may permit title to shares of any class to be issued or held otherwise than by a certificate and to be transferred by means of a "relevant system" (i.e., the CREST System) without a certificate.

The board of directors may take such steps as it sees fit in relation to the evidencing of and transfer of title to uncertificated shares, any records relating to the holding of uncertificated shares and the conversion of uncertificated shares to certificated shares, or vice-versa.

The company may by notice to the holder of an uncertificated share, require that share to be converted into certificated form.

The board of directors may take such other action that the board considers appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of an uncertified share or otherwise to enforce a lien in respect of it.

Other Relevant Laws and Regulations

Mandatory Bid

(i) The Takeover Code will apply to the company for so long as its central management and control is considered to be in the United Kingdom. Under the Takeover Code, where:

(a) any person, together with persons acting in concert with him, acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares in which he is already interested, and in which persons acting in concert with him are interested) carry 30% or more of the voting rights of a company; or

(b) any person who, together with persons acting in concert with him, is interested in shares which in the aggregate carry not less than 30% of the voting rights of a company but does not hold shares carrying more than 50% of such voting rights and such person, or any person acting in concert with him, acquires an interest in any other shares which increases the percentage of shares carrying voting rights in which he is interested;

such person shall, except in limited circumstances, be obliged to extend offers, on the basis set out in Rules 9.3, 9.4 and 9.5 of the Takeover Code, to the holders of any class of equity share capital, whether voting or non-voting, and also to the holders of any other class of transferable securities carrying voting rights. Offers for different classes of equity share capital must be comparable; the Takeover Panel should be consulted in advance in such cases.

(ii) An offer under Rule 9 of the Takeover Code must be in cash and at the highest price paid for any interest in the shares by the person required to make an offer or any person acting in concert with him during the 12 months prior to the announcement of the offer.

(iii) Under the Takeover Code, a "concert party" arises where persons acting together pursuant to an agreement or understanding (whether formal or informal and whether or not in writing) actively cooperate, through the acquisition by them of an interest in shares in a company, to obtain or consolidate control of the company. "Control" means holding, or aggregate holdings, of an interest in shares carrying 30% or more of the voting rights of the company, irrespective of whether the holding or holdings give *de facto* control.

Squeeze-Out

(i) Under sections 979 to 982 of the Companies Act, if an offeror were to acquire, or unconditionally contract to acquire, not less than 90% of the ordinary shares of the company, it could then compulsorily acquire the remaining 10%. It would do so by sending a notice to outstanding shareholders telling them that it will compulsorily acquire their shares, provided that no such notice may be served after the end of: (a) the period of three months beginning with the day after the last day on which the offer can be accepted; or (b) if earlier, and the offer is not one to which section 943(1) of the Companies Act applies, the period of six months beginning with the date of the offer.

(ii) Six weeks following service of the notice, the offeror must send a copy of it to the company together with the consideration for the ordinary shares to which the notice relates, and an instrument of transfer executed on behalf of the outstanding shareholder(s) by a person appointed by the offeror.

(iii) The company will hold the consideration on trust for the outstanding shareholders.

Sell-out

(i) Sections 983 to 985 of the Companies Act also give minority shareholders in the company a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer relating to all the ordinary shares of the company is made at any time before the end of the period within which the offer could be accepted and the offeror held or had agreed to acquire not less than 90% of the ordinary shares, any holder of shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those shares. The offeror is required to give any shareholder notice of his right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period, or, if longer a period of three months from the date of the notice.

(ii) If a shareholder exercises his rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

Differences in Corporate Law

The applicable provisions of the Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and English law.

	England and Wales	**Delaware**
Number of Directors	Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act must also be followed, such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

	England and Wales	Delaware
Vacancies on the Board of Directors	Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.
Annual General Meeting	Under the Companies Act, a public limited company must hold an annual general meeting in each six-month period following the company's annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

	England and Wales	Delaware
Notice of General Meetings	Under the Companies Act, at least 21 days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.
Quorum	Subject to the provisions of a company's articles of association, the Companies Act provides that two shareholders present at a meeting (in person or by proxy) shall constitute a quorum.	The certificate of incorporation or bylaws may specify the number of shares, the holders of which shall be present or represented by proxy at any meeting in order to constitute a quorum, but in no event shall a quorum consist of less than one third of the shares entitled to vote at the meeting. In the absence of such specification in the certificate of incorporation or bylaws, a majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of stockholders.
Proxy	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

	England and Wales	Delaware
Issue of New Shares	Under the Companies Act, the directors of a company must not exercise any power to allot shares or grant rights to subscribe for, or to convert any security into, shares unless they are authorized to do so by the company's articles of association or by an ordinary resolution of the shareholders. Any authorization given must state the maximum amount of shares that may be allotted under it and specify the date on which it will expire, which must be not more than five years from the date the authorization was given. The authority can be renewed by a further resolution of the shareholders.	Under Delaware law, if the company's certificate of incorporation so provides, the directors have the power to authorize the issuance of additional stock. The directors may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the company or any combination thereof.
Preemptive Rights	Under the Companies Act, "equity securities," being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as "ordinary shares," or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the Companies Act, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

	England and Wales	Delaware
Liability of Directors and Officers	Under the Companies Act, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to (i) purchase and maintain insurance against such liability; (ii) provide a "qualifying third party indemnity," or an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted; and (iii) provide a "qualifying pension scheme indemnity," or an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan.	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for: • any breach of the director's duty of loyalty to the corporation or its stockholders; • acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; • intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or • any transaction from which the director derives an improper personal benefit.

	England and Wales	Delaware
Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (iii) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.

	England and Wales	Delaware
Shareholder Vote on Certain Transactions	The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: • the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the shareholders or creditors or class thereof present and voting, either in person or by proxy; and • the approval of the court.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.

	England and Wales	Delaware
Standard of Conduct for Directors	Under English law, a director owes various statutory and fiduciary duties to the company, including: • to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole; • to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; • to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred; • to exercise independent judgment; • to exercise reasonable care, skill and diligence; • not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and • to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

	England and Wales	Delaware
Stockholder Suits	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.	Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: • state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs shares thereafter devolved on the plaintiff by operation of law; and • allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or • state the reasons for not making the effort. Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Stock Exchange Listing

We have applied to list our ADSs on the Nasdaq Global Market under the symbol "BCYC."

Transfer Agent and Registrar of Shares

Our share register will be maintained by Computershare Investor Services plc upon the closing of this offering. The share register reflects only record owners of our ordinary shares. Holders of our ADSs will not be treated as our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the ordinary shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see "Description of American Depositary Shares" in this prospectus.

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

Citibank, N.A. has agreed to act as the depositary bank for the American Depositary Shares. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. American Depositary Shares are frequently referred to as "ADSs" and represent ownership interests in securities that are on deposit with the depositary bank. ADSs may be represented by certificates that are commonly known as "American Depositary Receipts" or "ADRs." The depositary bank typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A. (London), located at Citigroup Centre, Canary Wharf, London, E14 5LB, United Kingdom.

We will appoint Citibank as depositary bank pursuant to a deposit agreement. A copy of the deposit agreement will be on file with the SEC under cover of a Registration Statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov).

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety. The portions of this summary description that are italicized describe matters that may be relevant to the ownership of ADSs but that may not be contained in the deposit agreement.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, one ordinary share that is on deposit with the depositary bank and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary bank or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary bank may agree to change the ADS-to-Share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary bank and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary bank, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary bank, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary bank, and the depositary bank (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary bank. As an ADS holder you appoint the depositary bank to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws in the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary bank, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary bank will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary bank only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary bank's services are made available to you. As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary bank in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary bank (commonly referred to as the "direct registration system" or "DRS"). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary bank. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary bank to the holders of the ADSs. The direct registration system includes automated transfers between the depositary bank and The Depository Trust Company ("DTC"), the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary bank or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary bank or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary bank or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction of the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary bank will arrange for the funds received in a currency other than U.S. dollars to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to English laws and regulations.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary bank will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary bank will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary bank holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will *either* distribute to holders new ADSs representing the ordinary shares deposited *or* modify the ADS-to-ordinary-share ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary-share ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary bank may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (*e.g.*, the U.S. securities laws) or if it is not operationally practicable. If the depositary bank does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to subscribe for additional ordinary shares, we will give prior notice to the depositary bank and we will assist the depositary bank in determining whether it is lawful and reasonably practicable to distribute rights to subscribe for additional ADSs to holders.

The depositary bank will establish procedures to distribute rights to subscribe for additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary bank is not obligated

to establish procedures to facilitate the distribution and exercise by holders of rights to subscribe for new ordinary shares other than in the form of ADSs.

The depositary bank will *not* distribute the rights to you if:

- We do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- We fail to deliver satisfactory documents to the depositary bank; or
- It is not reasonably practicable to distribute the rights.

The depositary bank will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary bank is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary bank and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary bank in determining whether such distribution is lawful and reasonably practicable.

The depositary bank will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary bank will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to subscribe for additional ordinary shares, we will notify the depositary bank in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary bank in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide to the depositary bank all of the documentation contemplated in the deposit agreement, the depositary bank will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary bank may sell all or a portion of the property received.

The depositary bank will *not* distribute the property to you and will sell the property if:

- We do not request that the property be distributed to you or if we request that the property not be distributed to you; or
- We do not deliver satisfactory documents to the depositary bank; or
- The depositary bank determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary bank in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary bank will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary bank will convert into U.S. dollars upon the terms of the deposit agreement the redemption funds received in a currency other than U.S. dollars and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary bank. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a *pro rata* basis, as the depositary bank may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the Company.

If any such change were to occur, your ADSs would, to the extent permitted by law and the deposit agreement, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary bank may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depositary bank may not lawfully distribute such property to you, the depositary bank may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

Upon completion of the offering, the ordinary shares being offered pursuant to the prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will issue ADSs to the underwriters named in the prospectus. After the completion of the offering, the ordinary shares that are being offered for sale pursuant to the prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will issue ADSs to the underwriters named in the prospectus.

After the closing of the offer, the depositary bank may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary bank will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by U.S. and English legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary bank or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary bank will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary bank. As such, you will be deemed to represent and warrant that:

- The ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained.
- All preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised.
- You are duly authorized to deposit the ordinary shares.
- The ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement).
- The ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary bank may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary bank and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary bank deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary bank with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depositary bank for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by U.S. and English law considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary bank the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary bank may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary bank may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares

represented by your ADSs may be delayed until the depositary bank receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary bank will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time except for:

- Temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends.
- Obligations to pay fees, taxes and similar charges.
- Restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary bank to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "Description of Share Capital and Articles of Association."

At our request, the depositary bank will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary bank to exercise the voting rights of the securities represented by ADSs. In lieu of distributing such materials, the depositary bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

If the depositary bank timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs as follows:

- *In the event of voting by show of hands*, the depositary bank will vote (or cause the custodian to vote) all ordinary shares held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- *In the event of voting by poll*, the depositary bank will vote (or cause the Custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except (a) as set forth above in the case voting is by show of hands, (b) in the event of voting by poll, holders of ADSs in respect of which no timely voting instructions have been received shall be deemed to have instructed the depositary to give a discretionary proxy to a person designated by us to vote the ordinary shares represented by such holders' ADSs; provided, however, that no such discretionary proxy shall be given with respect to any matter to be voted upon as to which we inform the depositary that (i) we do not wish such proxy to be given, (ii) substantial opposition exists, or (iii) the rights of holders of ordinary shares may be adversely affected, and (c) as otherwise contemplated in the deposit agreement). Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities

on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

Service	Fees
• Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary-share(s) ratio, or for any other reason), excluding ADS issuances as a result of distributions of shares)	Up to U.S. 5¢ per ADS issued
• Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property, upon a change in the ADS(s)-to-ordinary-share(s) ratio, or for any other reason)	Up to U.S. 5¢ per ADS cancelled
• Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to U.S. 5¢ per ADS held
• Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to U.S. 5¢ per ADS held
• Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to U.S. 5¢ per ADS held
• ADS Services	Up to U.S. 5¢ per ADS held on the applicable record date(s) established by the depositary bank
• Registration of ADS transfers (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and *vice versa*, or for any other reason)	Up to U.S. 5¢ per ADS (or fraction thereof) transferred
• Conversion of ADSs of one series for ADSs of another series (e.g., upon conversion of Partial Entitlement ADSs for Full Entitlement ADSs, or upon conversion of Restricted ADSs (each as defined in the Deposit Agreement) into freely transferable ADSs, and *vice versa*).	Up to U.S. 5¢ per ADS (or fraction thereof) converted

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary bank or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;

- the fees, expenses, spreads, taxes and other charges of the depositary bank and/or service providers (which may be a division, branch or affiliate of the depositary bank) in the conversion of foreign currency;

- the reasonable and customary out-of-pocket expenses incurred by the depositary bank in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and

- the fees, charges, costs and expenses incurred by the depositary bank, the custodian, or any nominee in connection with the ADR program.

ADS fees and charges for (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person for whom the ADSs are issued (in the case of ADS issuances) and to the person for whom ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary bank into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the ADS holder whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

In the event of refusal to pay the depositary bank fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary bank fees from any distribution to be made to the ADS holder. Certain depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of the ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary bank. You will receive prior notice of such changes. The depositary bank may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary bank agree from time to time.

Amendments and Termination

We may agree with the depositary bank to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for

book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary bank to terminate the deposit agreement. Similarly, the depositary bank may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary bank must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

After termination, the depositary bank will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary bank will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary bank will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with any termination of the deposit agreement, the depositary bank may make available to owners of ADSs a means to withdraw the ordinary shares represented by ADSs and to direct the depositary of such ordinary shares into an unsponsored American depositary share program established by the depositary bank. The ability to receive unsponsored American depositary shares upon termination of the deposit agreement would be subject to satisfaction of certain U.S. regulatory requirements applicable to the creation of unsponsored American depositary shares and the payment of applicable depositary fees.

Books of Depositary

The depositary bank will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary bank will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary bank's obligations to you. Please note the following:

- We and the depositary bank are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary bank disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary bank disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or

for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.

- We and the depositary bank will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary bank disclaim any liability if we or the depositary bank are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Incorporation, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary bank disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Incorporation or in any provisions of or governing the securities on deposit.
- We and the depositary bank further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary bank also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary bank may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary bank also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.
- Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among us, the depositary bank and you as ADS holder.
- Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary bank and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell

any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary bank may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary bank and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary bank and to the custodian proof of taxpayer status and residence and such other information as the depositary bank and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary bank and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary bank will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary bank may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement, the ADRs and the ADSs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) is governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs AGAINST US AND/OR THE DEPOSITARY BANK. IF WE OR THE DEPOSITARY OPPOSED A JURY TRIAL DEMAND BASED ON THE WAIVER, THE COURT WOULD DETERMINE WHETHER THE WAIVER WAS ENFORCEABLE IN THE FACTS AND CIRCUMSTANCES OF THAT CASE IN ACCORDANCE WITH APPLICABLE CASE LAW. HOWEVER, YOU WILL NOT BE DEEMED BY AGREEING TO THE TERMS OF THE DEPOSIT AGREEMENT TO HAVE WAIVED OUR OR THE DEPOSITARY'S COMPLIANCE WITH U.S. FEDERAL SECURITIES LAWS AND THE RULES AND REGULATIONS PROMULGATED THEREUNDER.

SHARES AND AMERICAN DEPOSITARY SHARES ELIGIBLE FOR FUTURE SALE

Upon completion of this offering, we will have 4,333,333 ADSs outstanding representing approximately 24.5% of our ordinary shares (or 4,983,333 ADSs outstanding representing approximately 27.5% of our ordinary shares, if the underwriters exercise in full their option to purchase additional ADSs), based on the number of ordinary shares outstanding as of March 31, 2019. All of the ADSs sold in this offering and the ordinary shares they represent will be freely transferable by persons other than our "affiliates" without restriction or further registration under the Securities Act. Rule 144 under the Securities Act defines an "affiliate" of a company as a person that, directly or indirectly, through one or more intermediaries, controls or is controlled by, or is under common control with, our company. All outstanding ordinary shares prior to this offering are "restricted securities" as that term is defined in Rule 144 because they were issued in a transaction or series of transactions not involving a public offering. Restricted securities, in the form of ADSs or otherwise, may be sold only if they are the subject of an effective registration statement under the Securities Act or if they are sold pursuant to an exemption from the registration requirement of the Securities Act such as those provided for in Rule 144 or 701 promulgated under the Securities Act, which rules are summarized below. Restricted ordinary shares may also be sold outside of the United States to non-U.S. persons in accordance with Rule 904 of Regulation S under the Securities Act. This prospectus may not be used in connection with any resale of the ADSs acquired in this offering by our affiliates.

Sales of substantial amounts of the ADSs in the public market could materially and adversely affect prevailing market prices of the ADSs. Prior to this offering, there has been no public market for our ordinary shares or ADSs, and while we have applied to list the ADSs on the Nasdaq, we cannot assure you that a regular trading market will develop in the ADSs. We do not expect that a trading market will develop for our ordinary shares not represented by ADSs.

Lock-up Agreements

In connection with this offering, all of our directors and executive officers and certain holders of our shares, who collectively held substantially all ordinary shares (assuming conversion of all of our outstanding convertible preferred shares, issuance of the bonus shares and exercise of the warrants) as of March 31, 2019, and substantially all of our optionholders who are not shareholders, have signed lock-up agreements which, subject to certain exceptions, prevent them from selling any of our ordinary shares or ADSs, or any securities convertible into or exercisable or exchangeable for ordinary shares or ADSs for a period of not less than 180 days from the date of this prospectus without the prior written consent of each of the representatives. The representatives may in their sole discretion and at any time without notice release some or all of the shares or ADSs subject to lock-up agreements prior to the expiration of the 180-day period. When determining whether or not to release shares or ADSs from the lock-up agreements, the representatives may consider, among other factors, the shareholder's reasons for requesting the release, the number of shares or ADSs for which the release is being requested and market conditions at the time. In addition, our optionholders who have not executed lock-up agreements are nevertheless subject to similar restrictions set forth in their respective option agreements.

Rule 144

In general, under Rule 144 as currently in effect, a person who has beneficially owned our restricted securities for at least six months is entitled to sell the restricted securities without registration under the Securities Act, subject to certain restrictions. Persons who are our affiliates (which may include persons beneficially owning 10% or more of our outstanding shares) may sell

within any three-month period a number of restricted securities that does not exceed the greater of the following:

- 1% of the number of our ordinary shares then outstanding, in the form of ADSs or otherwise, which will equal approximately 176,964 ordinary shares immediately after this offering; and
- the average weekly trading volume of the ordinary shares, in the form of ADSs or otherwise, on Nasdaq during the four calendar weeks preceding the date on which notice of the sale is filed with the SEC.

Such sales are also subject to manner-of-sale provisions, notice requirements and the availability of current public information about us.

In general, under Rule 144 as currently in effect, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, persons who are not our affiliates and have beneficially owned our restricted securities for more than six months but not more than one year may sell the restricted securities without registration under the Securities Act subject to the availability of current public information about us. Persons who are not our affiliates and have beneficially owned our restricted securities for more than one year may freely sell the restricted securities without registration under the Securities Act.

Rule 701

Beginning 90 days after the date of this prospectus, persons other than affiliates who purchased ordinary shares under a written compensatory plan or contract may be entitled to sell such shares in the United States in reliance on Rule 701 under the Securities Act, or Rule 701. Rule 701 permits affiliates to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. Rule 701 further provides that non-affiliates may sell these shares in reliance on Rule 144 subject only to its manner-of-sale requirements. However, the Rule 701 shares would remain subject to any applicable lock-up arrangements and would only become eligible for sale when the lock-up period expires.

Registration Rights

Upon completion of this offering, certain holders of our ordinary shares or their transferees will be entitled to request that we register their ordinary shares under the Securities Act, following the expiration of the lock-up agreements described above. See "Description of Share Capital and Articles of Association — Registration Rights."

Share Option Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our share option plans or independent options. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of March 31, 2019, we estimate that such registration statement on Form S-8 will cover approximately 4,836,828 shares.

MATERIAL INCOME TAX CONSIDERATIONS

The following summary contains a description of material U.K. and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs. This summary should not be considered a comprehensive description of all the tax considerations that may be relevant to the decision to acquire ordinary shares or ADSs in this offering.

Material United States Federal Income Tax Considerations for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our ordinary shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire securities. This discussion applies only to a U.S. Holder that is an initial purchaser of the ordinary shares or ADSs pursuant to the offering and that holds our ordinary shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired our ordinary shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons holding our ordinary shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States; and
- persons who own (directly or through attribution) 10% or more (by vote or value) of our outstanding ordinary shares.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares or ADSs and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of holding and disposing of ordinary shares or ADSs.

The discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein — possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares or ADSs and is:

(i) An individual who is a citizen or individual resident of the United States;

(ii) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

(iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

Generally, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADS. Accordingly, no gain or loss will be recognized upon an exchange of ADSs for ordinary shares.

PERSONS CONSIDERING AN INVESTMENT IN ORDINARY SHARES OR ADSs SHOULD CONSULT THEIR OWN TAX ADVISORS AS TO THE PARTICULAR TAX CONSEQUENCES APPLICABLE TO THEM RELATING TO THE ACQUISITION, OWNERSHIP AND DISPOSITION OF THE ORDINARY SHARES OR ADSs, INCLUDING THE APPLICABILITY OF U.S. FEDERAL, STATE AND LOCAL TAX LAWS.

PFIC Rules

If we are classified as a PFIC in any taxable year, a U.S. Holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

Based on our analysis of our income, assets, activities and market capitalization, we believe that we were a PFIC in the 2018 taxable year. We have not yet determined our PFIC status for the current taxable year, but we may be a PFIC. A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year, and we may be classified as a PFIC currently or in the future. The total value of our assets for purposes of the asset test generally will be calculated using the market price

of the ordinary shares or ADSs, which may fluctuate considerably. Fluctuations in the market price of the ordinary shares or ADSs may result in our being a PFIC for any taxable year. Because of the uncertainties involved in establishing our PFIC status, there can be no assurance regarding if we currently are treated as a PFIC, or may be treated as a PFIC in the future.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules, or (ii) the U.S. Holder makes a Qualified Electing Fund Election, or QEF Election, with respect to all taxable years during such U.S. Holders holding period in which we are a PFIC. If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the ordinary shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an actual sale or other disposition of the ordinary shares or ADSs. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

For each taxable year we are treated as a PFIC with respect to U.S. Holders, U.S. Holders will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including, under certain circumstances, a pledge) of ordinary shares or ADSs, unless (i) such U.S. Holder makes a QEF Election or (ii) our ordinary shares or ADSs constitute "marketable" securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder's holding period for the ordinary shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over a U.S. Holder's holding period for the ordinary shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares or ADSs cannot be treated as capital, even if a U.S. Holder holds the ordinary shares or ADSs as capital assets.

In addition, if we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the stock of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

If a U.S. Holder makes an effective QEF Election, the U.S. Holder will be required to include in gross income each year, whether or not we make distributions, as capital gains, such U.S. Holder's

pro rata share of our net capital gains and, as ordinary income, such U.S. Holder's pro rata share of our earnings in excess of our net capital gains. If we determine that we are a PFIC for this year or any future taxable year, we currently expect that we would provide the information necessary for U.S. Holders to make a QEF Election.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares or ADSs by making a mark-to-market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable." Ordinary shares or ADSs will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs will be listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on Nasdaq and are regularly traded, and you are a holder of ADSs, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC. Each U.S. Holder should consult its tax advisor as to the whether a mark-to-market election is available or advisable with respect to the ordinary shares or ADSs.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the ordinary shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the ordinary shares or ADSs. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares or ADSs over the fair market value of the ordinary shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the ordinary shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the Internal Revenue Service, or the IRS, unless the ordinary shares or ADSs cease to be marketable.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our ordinary shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs AS WELL AS

THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Taxation of Distributions

Subject to the discussion above under "PFIC rules," distributions paid on ordinary shares or ADSs, other than certain pro rata distributions of ordinary shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations and the discussions above regarding concerns expressed by the U.S. Treasury, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income" if we are a "qualified foreign corporation" and certain other requirements are met. However, the qualified dividend income treatment may not apply if we are treated as a PFIC with respect to the U.S. Holder. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. Because no U.K. income taxes will be withheld from dividends on ordinary shares or ADSs, there will be no creditable foreign taxes associated with any dividends that a U.S. Holder will receive. The rules governing foreign tax credits are complex and U.S. Holders should therefore consult their tax advisers regarding the effect of the receipt of dividends for foreign tax credit limitation purposes.

Sale or Other Taxable Disposition of Ordinary Shares and ADSs

Subject to the discussion above under "PFIC rules," gain or loss realized on the sale or other taxable disposition of ordinary shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares or ADSs are treated as traded on an "established securities market" and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount

received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding on a duly executed IRS Form W-9 or otherwise establishes an exemption.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle the U.S. Holder to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions), by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed. U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares or ADSs.

U.K. Taxation

The following is intended as a general guide to current U.K. tax law and HM Revenue & Customs, or HMRC, published practice applying as at the date of this prospectus (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ADSs. It does not constitute legal or tax advice and does not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ADSs, or all of the circumstances in which holders of ADSs may benefit from an exemption or relief from U.K. taxation. It is written on the basis that the company does not (and will not) derive 75% or more of its qualifying asset value from U.K. land, and that the company is and remains solely resident in the U.K. for tax purposes and will therefore be subject to the U.K. tax regime and not the U.S. tax regime save as set out above under "Material United States Federal Income Tax Considerations for U.S. Holders".

Except to the extent that the position of non-U.K. resident persons is expressly referred to, this guide relates only to persons who are resident (and, in the case of individuals, domiciled or deemed domiciled) for tax purposes solely in the U.K. and do not have a permanent establishment, branch, agency (or equivalent) or fixed base in any other jurisdiction with which the holding of the ADSs is connected, or U.K. Holders, who are absolute beneficial owners of the ADSs (and do not hold the ADSs through an Individual Savings Account or a Self-Invested Personal Pension) and who hold the ADSs as investments.

This guide may not relate to certain classes of U.K. Holders, such as (but not limited to):

- persons who are connected with the company;
- financial institutions;
- insurance companies;
- charities or tax-exempt organizations;
- collective investment schemes;
- pension schemes;
- market makers, intermediaries, brokers or dealers in securities;
- persons who have (or are deemed to have) acquired their ADSs by virtue of an office or employment or who are or have been officers or employees of the company or any of its affiliates; and
- individuals who are subject to U.K. taxation on a remittance basis.

Based on published HMRC guidance we would expect that HMRC will regard a holder of ADSs as holding the beneficial interest in the underlying shares and therefore these paragraphs assume that a holder of ADSs is the beneficial owner of the underlying ordinary shares and any dividends paid in respect of the underlying ordinary shares (where the dividends are regarded for U.K. purposes as that person's own income) for U.K. direct tax purposes.

THESE PARAGRAPHS ARE A SUMMARY OF CERTAIN U.K. TAX CONSIDERATIONS AND ARE INTENDED AS A GENERAL GUIDE ONLY. IT IS RECOMMENDED THAT ALL HOLDERS OF ADSs OBTAIN ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF THE ADSs IN THEIR OWN PARTICULAR CIRCUMSTANCES FROM THEIR OWN TAX ADVISORS. IN PARTICULAR, NON-U.K. RESIDENT OR DOMICILED PERSONS ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION AGREEMENTS.

Dividends

Withholding Tax

Dividends paid by the company will not be subject to any withholding or deduction for or on account of U.K. tax.

Income Tax

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the company. An individual holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. income tax on dividends received from the company unless he or she carries on (whether solely or in partnership) a trade, profession or vocation in the U.K. through a permanent establishment, branch or agency to which the ADSs are attributable. There are certain exceptions for trading in the UK through independent agents, such as some brokers and investment managers.

All dividends received by an individual U.K. Holder from us or from other sources will form part of that U.K. Holder's total income for income tax purposes and will constitute the top slice of that income. A nil rate of income tax will apply to the first £2,000 of taxable dividend income received by the individual U.K. Holder in a tax year. Income within the nil rate band will be taken into account in determining whether income in excess of the £2,000 tax-free allowance falls within the basic rate, higher rate or additional rate tax bands. Dividend income in excess of the tax-free

allowance will (subject to the availability of any income tax personal allowance) be taxed at 7.5% to the extent that the excess amount falls within the basic rate tax band, 32.5% to the extent that the excess amount falls within the higher rate tax band and 38.1% to the extent that the excess amount falls within the additional rate tax band.

Corporation Tax

A corporate holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. corporation tax on dividends received from the company unless it carries on (whether solely or in partnership) a trade in the United Kingdom through a permanent establishment to which the ADSs are attributable.

Corporate U.K. Holders should not be subject to U.K. corporation tax on any dividend received from the company so long as the dividends qualify for exemption, which should be the case, although certain conditions must be met. If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the amount of any dividends (at the current rate of 19%).

Chargeable Gains

A disposal or deemed disposal of ADSs by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs (such as the annual exemption), give rise to a chargeable gain or an allowable loss for the purposes of U.K. capital gains tax and corporation tax on chargeable gains.

If an individual U.K. Holder who is subject to U.K. income tax at either the higher or the additional rate is liable to U.K. capital gains tax on the disposal of ADSs, the applicable rate will be 20% (2019/2020). For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and liable to U.K. capital gains tax on such disposal, the applicable rate would be 10% (2019/2020), save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the rate applicable to the excess would be 20% (2019/2020).

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal (or deemed disposal) of ADSs, the main rate of U.K. corporation tax (currently 19%) would apply. Indexation allowance is not available in respect of disposals of ADSs acquired on or after January 1, 2018 (and only covers the movement in the retail prices index up until December 31, 2017, in respect of assets acquired prior to that date).

A holder of ADSs which is not resident for tax purposes in the United Kingdom should not normally be liable to U.K. capital gains tax or corporation tax on chargeable gains on a disposal (or deemed disposal) of ADSs, unless the person is carrying on (whether solely or in partnership) a trade, profession or vocation in the United Kingdom through a permanent establishment, branch or agency to which the ADSs are attributable. However, an individual holder of ADSs who has ceased to be resident for tax purposes in the United Kingdom for a period of less than five years and who disposes of ADSs during that period may be liable on his or her return to the United Kingdom to U.K. tax on any capital gain realized (subject to any available exemption or relief).

Stamp Duty and Stamp Duty Reserve Tax

The discussion below relates to the holders of our ordinary shares or ADSs wherever resident, however it should be noted that special rules may apply to certain persons such as market makers, brokers, dealers or intermediaries.

Issue of Ordinary Shares

No U.K. stamp duty or stamp duty reserve tax, or SDRT, is payable on the issue of the underlying ordinary shares in the company.

Transfers of Ordinary Shares

An unconditional agreement to transfer ordinary shares will normally give rise to a charge to SDRT at the rate of 0.5% of the amount or value of the consideration payable for the transfer. The purchaser of the shares is liable for the SDRT. Transfers of ordinary shares in certificated form are generally also subject to stamp duty at the rate of 0.5% of the amount or value of the consideration given for the transfer (rounded up to the next £5.00). Stamp duty is normally paid by the purchaser. The charge to SDRT will be cancelled or, if already paid, repaid (generally with interest), where a transfer instrument has been duly stamped within six years of the charge arising, (either by paying the stamp duty or by claiming an appropriate relief) or if the instrument is otherwise exempt from stamp duty.

An unconditional agreement to transfer ordinary shares to, or to a nominee or agent for, a person whose business is or includes the issue of depositary receipts or the provision of clearance services will generally be subject to SDRT (and, where the transfer is effected by a written instrument, stamp duty) at a higher rate of 1.5% of the amount or value of the consideration given for the transfer unless the clearance service has made and maintained an election under section 97A of the U.K. Finance Act 1986, or a section 97A election. It is understood that HMRC regards the facilities of DTC as a clearance service for these purposes and we are not aware of any section 97A election having been made by the DTC.

Based on current published HMRC practice and recent case law in respect of the European Council Directives 69/335/EEC and 2009/7/EC, or the Capital Duties Directives, no SDRT is generally payable where the transfer of ordinary shares to a clearance service or depositary receipt system outside the European Union is an integral part of an issue of share capital (although the relevant judgment refers to transfers which are integral to the raising of capital). In addition, a recent Court of Justice of the European Union judgment (Air Berlin plc v. HMRC (2017)) held on the relevant facts that the Capital Duties Directives preclude the taxation of a transfer of legal title to shares for the sole purpose of listing those shares on a stock exchange which does not impact the beneficial ownership of the shares, but, as yet, the U.K. domestic law and HMRC's published practice remain unchanged and, accordingly, we anticipate that amounts account of SDRT will continue to be collected by the depositary receipt issuer or clearance service. Holders of ordinary shares should consult their own independent professional advisers before incurring or reimbursing the costs of such a 1.5% SDRT charge.

Any stamp duty or SDRT payable on a transfer of ordinary shares to a depositary receipt system or clearance service will in practice generally be paid by the participants in the clearance service or depositary receipt system.

Issue or Transfers of ADSs

No U.K. stamp duty or SDRT is payable on the issue or transfer of (including an agreement to transfer) ADSs in the Company.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the ADSs being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of ADSs indicated in the following table. Goldman Sachs & Co. LLC, Jefferies LLC and Piper Jaffray & Co. are the representatives of the underwriters.

Underwriters	Number of ADSs
Goldman Sachs & Co. LLC	
Jefferies LLC	
Piper Jaffray & Co.	
Canaccord Genuity LLC	
Total	4,333,333

The underwriters are committed to take and pay for all of the ADSs being offered, if any are taken, other than the ADSs covered by the option described below unless and until this option is exercised. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters have an option to buy up to an additional 650,000 ADSs from us to cover sales by the underwriters of a greater number of ADSs than the total number set forth in the table above. They may exercise that option for 30 days. If any ADSs are purchased pursuant to this option, the underwriters will severally purchase ADSs in approximately the same proportion as set forth in the table above.

The following table shows the per ADS and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to 650,000 additional ADSs from us.

	No Exercise	Full Exercise
Per ADS	$	$
Total	$	$

ADSs sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any ADSs sold by the underwriters to securities dealers may be sold at a discount of up to $ per ADS from the initial public offering price. After the initial offering of the ADSs, the representatives may change the offering price and the other selling terms. The offering of the ADSs by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part. Sales of ADSs made outside of the United States may be made by affiliates of the underwriters.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of ADSs to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make internet distributions on the same basis as other allocations.

We and our executive officers, directors, and holders of substantially all of our equity securities and securities convertible into or exchangeable for our equity securities have agreed or will agree with the underwriters, subject to certain exceptions, not to dispose of or hedge any of our or their equity securities or securities convertible into or exchangeable for equity securities during the

period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior written consent of the representatives.

Certain of our existing shareholders and their affiliated entities, including those affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $25.0 million of ADSs in this offering at the initial public offering price per ADS and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no ADSs to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no ADSs in this offering. The underwriters will receive the same underwriting discount and commissions on these ADSs as they will on any other ADSs sold to the public in this offering.

Prior to the offering, there has been no public market for the ADSs. The initial public offering price was negotiated among us and the representatives. Among the factors considered in determining the initial public offering price of the ADSs, in addition to prevailing market conditions, were our historical performance, estimates of our business potential and earnings prospects, an assessment of our management and the consideration of the above factors in relation to market valuation of companies in related businesses.

We have applied to list the ADSs on the Nasdaq Global Market under the symbol "BCYC."

In connection with the offering, the underwriters may purchase and sell ADSs in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of ADSs than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional ADSs for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional ADSs or purchasing ADSs in the open market. In determining the source of ADSs to cover the covered short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared to the price at which they may purchase additional ADSs pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional ADSs for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the ADSs in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of ADSs made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased ADSs sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our ADSs, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the ADSs. As a result, the price of the ADSs may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on the Nasdaq Global Market, in the over-the-counter market or otherwise.

We estimate that the expenses payable by us in this offering, excluding underwriting discounts and commissions, will be approximately $3.4 million. We have agreed to reimburse the underwriters for certain of their expenses in an amount up to $35,000.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively traded securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities or instruments of the issuer (directly, as collateral securing other obligations or otherwise) or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of our securities may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our securities may be made at any time under the following exemptions under the Prospectus Directive:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the Representatives for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of our securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to public" in relation to our securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our securities to be offered so as to enable an investor to decide to purchase our securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, and the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

Solely for the purposes of the product governance requirements contained within: (a) EU Directive 2014/65/EU on markets in financial instruments, as amended, or MiFID II; (b) Articles 9 and 10 of Commission Delegated Directive (European Union) 2017/593 supplementing MiFID II; and (c) local implementing measures (together, the "MiFID II Product Governance Requirements"), and disclaiming all and any liability, whether arising in tort, contract or otherwise, which any "manufacturer" for the purposes of the MiFID II Product Governance Requirements may otherwise have with respect thereto, the ADSs which are the subject of this offering have been subject to a product approval process, which has determined that such securities are: (i) compatible with an end target market of retail investors and investors who meet the criteria of professional clients and eligible counterparties, each as defined in MiFID II; and (ii) eligible for distribution through all distribution channels as are permitted by MiFID II, or the Target Market Assessment.

Notwithstanding the Target Market Assessment, distributors should note that: the price of the ADSs may decline and investors could lose all or part of their investment; the ADSs offer no guaranteed income and no capital protection; and an investment in the ADSs is compatible only with investors who do not need a guaranteed income or capital protection, who, either alone or in conjunction with an appropriate financial or other adviser, are capable of evaluating the merits and risks of such an investment and who have sufficient resources to be able to bear any losses that may result therefrom. For the avoidance of doubt, the Target Market Assessment does not constitute: (a) an assessment of suitability or appropriateness for the purposes of MiFID II; or (b) a recommendation to any investor or group of investors to invest in, or purchase, or take any other action whatsoever with respect to the ADSs. Each distributor is responsible for undertaking its own target market assessment in respect of the ADSs and determining appropriate distribution channels.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed at qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as "relevant persons"). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged in with relevant persons. Any person who is not a relevant person should not act or rely on this prospectus or any of its contents.

Canada

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted

clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The securities may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the securities may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after

that corporation has acquired the securities under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32").

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the securities under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Solely for the purposes of its obligations pursuant to Section 309B of the SFA, we have determined, and hereby notify all relevant persons (as defined in the CMP Regulations 2018), that the shares are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering. This offering document does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the securities may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the securities without disclosure to investors under Chapter 6D of the Corporations Act.

The securities applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an

exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring securities must observe such Australian on-sale restrictions.

This offering document contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this offering document is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Dubai International Financial Centre

This offering document relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This offering document is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth in this prospectus and has no responsibility for the offering document. The securities to which this offering document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this offering document you should consult an authorized financial advisor.

Switzerland

We have not and will not register with the Swiss Financial Market Supervisory Authority ("FINMA") as a foreign collective investment scheme pursuant to Article 119 of the Federal Act on Collective Investment Scheme of 23 June 2006, as amended ("CISA"), and accordingly the securities being offered pursuant to this prospectus have not and will not be approved, and may not be licenseable, with FINMA. Therefore, the securities have not been authorized for distribution by FINMA as a foreign collective investment scheme pursuant to Article 119 CISA and the securities offered hereby may not be offered to the public (as this term is defined in Article 3 CISA) in or from Switzerland. The securities may solely be offered to "qualified investors," as this term is defined in Article 10 CISA, and in the circumstances set out in Article 3 of the Ordinance on Collective Investment Scheme of 22 November 2006, as amended ("CISO"), such that there is no public offer. Investors, however, do not benefit from protection under CISA or CISO or supervision by FINMA. This prospectus and any other materials relating to the securities are strictly personal and confidential to each offeree and do not constitute an offer to any other person. This prospectus may only be used by those qualified investors to whom it has been handed out in connection with the offer described in this prospectus and may neither directly or indirectly be distributed or made available to any person or entity other than its recipients. It may not be used in connection with any other offer and shall in particular not be copied and/or distributed to the public in Switzerland or from Switzerland. This prospectus does not constitute an issue prospectus as that term is understood pursuant to Article 652a and/or 1156 of the Swiss Federal Code of Obligations. We have not applied for a listing of the securities on the SIX Swiss Exchange or any other regulated securities market in Switzerland, and consequently, the information presented in this prospectus does not necessarily comply with the information standards set out in the listing rules of the SIX Swiss Exchange and corresponding prospectus schemes annexed to the listing rules of the SIX Swiss Exchange.

LEGAL MATTERS

The validity of our ADSs and certain other matters of English law and U.S. federal law will be passed upon for us by Goodwin Procter LLP. Legal counsel to the underwriters in connection with this offering are Cooley LLP.

EXPERTS

The financial statements as of December 31, 2017 and 2018 and for the years then ended included in this prospectus have been so included in reliance on the report (which contains an explanatory paragraph relating to the Company's restatement of previously issued financial statements as described in Note 1 to the consolidated financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The registered business address of PricewaterhouseCoopers LLP is 1 Embankment Place, London, WC2N 6RH, United Kingdom.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated and currently existing under the laws of England and Wales. In addition, certain of our directors and officers reside outside of the United States and most of the assets of our non-U.S. subsidiaries are located outside of the United States. As a result, it may be difficult for investors to effect service of process on us or those persons in the United States or to enforce in the United States judgments obtained in United States courts against us or those persons based on the civil liability or other provisions of the United States securities laws or other laws.

In addition, uncertainty exists as to whether the courts of England and Wales would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liabilities provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in England and Wales against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

We have been advised by Goodwin Procter LLP that there is currently no treaty between (i) the United States and (ii) England and Wales providing for reciprocal recognition and enforcement of judgments of United States courts in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards) and that a final judgment for the payment of money rendered by any general or state court in the United States based on civil liability, whether predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. We have also been advised by Goodwin Procter LLP that any final and conclusive monetary judgment for a definite sum obtained against us in United States courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that:

- the relevant U.S. court had jurisdiction over the original proceedings according to English conflicts of laws principles at the time when proceedings were initiated;
- England and Wales courts had jurisdiction over the matter on enforcement and we either submitted to such jurisdiction or were resident or carrying on business within such jurisdiction and were duly served with process;
- the U.S. judgment was final and conclusive on the merits in the sense of being final and unalterable in the court that pronounced it and being for a definite sum of money;
- the judgment given by the courts was not in respect of penalties, taxes, fines or similar fiscal or revenue obligations (or otherwise based on a U.S. law that an English court considers to relate to a penal, revenue or other public law);
- the judgment was not procured by fraud;
- recognition or enforcement of the judgment in England and Wales would not be contrary to public policy or the Human Rights Act 1998;
- the proceedings pursuant to which judgment was obtained were not contrary to natural justice;
- the U.S. judgment was not arrived at by doubling, trebling or otherwise multiplying a sum assessed as compensation for the loss or damages sustained and not being otherwise in breach of Section 5 of the U.K. Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under Section 1 of that Act;

- there is not a prior decision of an English court or the court of another jurisdiction on the issues in question between the same parties; and
- the English enforcement proceedings were commenced within the limitation period.

Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the United States securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision.

Subject to the foregoing, investors may be able to enforce in England and Wales judgments in civil and commercial matters that have been obtained from U.S. federal or state courts. Nevertheless, we cannot assure you that those judgments will be recognized or enforceable in England and Wales.

If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. In addition, it may not be possible to obtain an English judgment or to enforce that judgment if the judgment debtor is or becomes subject to any insolvency or similar proceedings, or if the judgment debtor has any set-off or counterclaim against the judgment creditor. Also note that, in any enforcement proceedings, the judgment debtor may raise any counterclaim that could have been brought if the action had been originally brought in England unless the subject of the counterclaim was in issue and denied in the U.S. proceedings.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (File Number 333-231076) under the Securities Act with respect to the ADSs we are offering by this prospectus. A related registration statement on Form F-6 will be filed with the SEC to register the ADSs. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and the ADSs, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the closing of the offering, we will be subject to the informational requirements of the Securities Exchange Act of 1934 and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at *www.sec.gov*.

We intend to furnish the depositary with our annual reports, which will include a review of operations and annual audited consolidated combined financial statements prepared in conformity with U.S. GAAP, and all notices of shareholders' meetings and other reports and communications that are made generally available to our shareholders. The depositary will make such notices, reports and communications available to holders of ADSs and will mail to all record holders of ADSs the information contained in any notice of a shareholders' meeting received by the depositary from us.

BICYCLE THERAPEUTICS LIMITED

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Index to Unaudited Interim Consolidated Financial Statements as of December 31, 2018 and March 31, 2019 and for the Three Month Periods Ended March 31, 2018 and 2019

Report of Independent Registered Public Accounting Firm

To the Board of Directors of Bicycle Therapeutics Limited

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Bicycle Therapeutics Limited and its subsidiaries (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, consolidated statements of convertible preferred shares and shareholders' (deficit) equity and consolidated statements of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Restatement of Previously Issued Financial Statements

As discussed in Note 1 to the consolidated financial statements, the Company has restated its 2017 financial statements to correct an error.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
Cambridge, United Kingdom
March 22, 2019, except for the effects of the corporate reorganization by way of a bonus share issuance having the effect of a share split as described in Note 1 to the consolidated financial statements, as to which the date is May 13, 2019

We have served as the Company's or its predecessor's auditor since 2010, which includes periods before the Company became subject to SEC reporting requirements.

Bicycle Therapeutics Limited

Consolidated Balance Sheets

(amounts in thousands, except share and per share data)

	December 31,	
	2017	2018
	(as restated)	
Assets		
Current assets:		
Cash	$ 67,663	$ 63,380
Accounts receivable	—	5,021
Prepaid expenses and other current assets	848	2,076
Research and development incentives receivable	3,001	6,292
Total current assets	71,512	76,769
Property and equipment, net	1,362	1,818
Other assets	1,127	3,039
Total assets	$ 74,001	$ 81,626
Liabilities, convertible preferred shares and shareholders' (deficit) equity		
Current liabilities:		
Accounts payable	$ 2,065	$ 1,887
Accrued expenses and other current liabilities	3,405	7,032
Deferred revenue, current portion	3,981	10
Total current liabilities	9,451	8,929
Warrant liability	4,411	4,804
Deferred revenue, net of current portion	10,486	14,625
Other long-term liabilities	396	897
Total liabilities	24,744	29,255
Commitments and contingencies (Note 12)		
Series A convertible preferred shares, £0.01 nominal value; 3,000,001 shares authorized at December 31, 2017 and 2018; 2,800,001 shares issued and outstanding at December 31, 2017 and 2018; liquidation value of $35,753 at December 31, 2018	41,820	41,820
Series B1 convertible preferred shares, £0.01 nominal value; 4,690,485 shares authorized at December 31, 2017 and 2018; 3,947,198 shares issued and outstanding at December 31, 2017 and 2018; liquidation value of $57,460 at December 31, 2018	54,621	54,621
Series B2 convertible preferred shares, £0.01 nominal value; no shares authorized at December 31, 2017 and 1,403,633 shares authorized at December 31, 2018; no shares issued and outstanding at December 31, 2017 and 1,323,248 issued and outstanding at December 31, 2018; liquidation value of $26,274 at December 31, 2018	—	25,756
Shareholders' (deficit) equity:		
Ordinary shares, £0.01 nominal value; 12,726,395 shares authorized at December 31, 2017 and 15,452,420 shares authorized at December 31, 2018; 531,461 and 898,675 shares issued at December 31, 2017 and December 31, 2018, respectively; 368,995 and 814,728 shares outstanding at December 31, 2017 and December 31, 2018, respectively	5	10
Additional paid-in capital	838	1,857
Accumulated other comprehensive income (loss)	69	(1,751)
Accumulated deficit	(48,096)	(69,942)
Total shareholders' (deficit) equity	(47,184)	(69,826)
Total liabilities, convertible preferred shares and shareholders' (deficit) equity	$ 74,001	$ 81,626

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2017	2018
	(as restated)	
Collaboration revenues	$ 2,060	$ 7,136
Operating expenses:		
Research and development	11,866	20,761
General and administrative	6,407	8,121
Total operating expenses	18,273	28,882
Loss from operations	(16,213)	(21,746)
Other income (expense):		
Interest and other income	50	169
Other expense	(119)	(665)
Total other expense, net	(69)	(496)
Net loss before income tax provision	(16,282)	(22,242)
Benefit from income taxes	(23)	(396)
Net loss	$ (16,259)	$ (21,846)
Net loss attributable to ordinary shareholders	$ (16,259)	$ (21,846)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (48.81)	$ (49.78)
Weighted average ordinary shares outstanding, basic and diluted	333,125	438,862
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted (unaudited)		$ (1.93)
Pro forma weighted average number of ordinary shares outstanding, basic and diluted (unaudited)		10,954,310
Comprehensives Loss:		
Net loss	$ (16,259)	$ (21,846)
Other comprehensive income (loss):		
Foreign currency translation adjustment	2,355	(1,820)
Total comprehensive loss	$ (13,904)	$ (23,666)

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited
Consolidated Statements of Convertible Preferred Shares and Shareholders' (Deficit) Equity
(In thousands, except share amounts)

	Series A Convertible Preferred Shares		Series B1 Convertible Preferred Shares		Series B2 Convertible Preferred Shares		Ordinary Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2016	2,800,001	$ 41,820	—	$ —	—	$ —	316,215	$ 4	$ 323	$ (2,286)	$ (31,837)	$ (33,796)
Issuance of convertible preferred shares, net of issuance costs of $587 and fair value of warrants to subscribe for convertible preferred shares of $3,254 (as restated)	—	—	3,947,198	54,621	—	—	—	—	—	—	—	—
Issuance of restricted share awards (as restated)	—	—	—	—	—	—	48,480	1	114	—	—	115
Issuance of ordinary shares upon exercise of share options	—	—	—	—	—	—	4,300	—	—	—	—	—
Share-based compensation expense (as restated)	—	—	—	—	—	—	—	—	401	—	—	401
Foreign currency translation adjustment (as restated)	—	—	—	—	—	—	—	—	—	2,355	—	2,355
Net loss (as restated)	—	—	—	—	—	—	—	—	—	—	(16,259)	(16,259)
Balance at December 31, 2017 (as restated)	2,800,001	41,820	3,947,198	54,621	—	—	368,995	5	838	69	(48,096)	(47,184)
Issuance of convertible preferred shares, net of issuance costs of $327	—	—	—	—	1,323,248	25,756	—	—	—	—	—	—
Issuance of restricted share awards	—	—	—	—	—	—	95,644	1	223	—	—	224
Issuance of ordinary shares in exchange for surrender of vested share options							340,728	4	(4)	—	—	—
Issuance of ordinary shares upon exercise of share options	—	—	—	—	—	—	9,361	—	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	800	—	—	800
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	(1,820)	—	(1,820)
Net loss	—	—	—	—	—	—	—	—	—	—	(21,846)	(21,846)
Balance at December 31, 2018	2,800,001	$ 41,820	3,947,198	$ 54,621	1,323,248	$ 25,756	814,728	$ 10	$ 1,857	$ (1,751)	$ (69,942)	$ (69,826)

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31, 2017 (as restated)	Year Ended December 31, 2018
Cash flows from operating activities:		
Net loss	$ (16,259)	$ (21,846)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	515	1,023
Depreciation and amortization	332	712
Non-cash research and development expense	856	—
Change in fair value of warrant liability	119	665
Changes in operating assets and liabilities:		
Accounts receivable	—	(400)
Research and development incentives receivable	(1,407)	(3,586)
Prepaid expenses and other current assets	(330)	(1,329)
Other assets	(1,039)	(301)
Accounts payable	67	(169)
Accrued expenses and other current liabilities	1,267	2,557
Deferred revenue	14,081	(3,947)
Other long-term liabilities	383	543
Net cash used in operating activities	(1,415)	(26,078)
Cash used in investing activities:		
Purchases of property and equipment	(1,113)	(1,186)
Net cash used in investing activities	(1,113)	(1,186)
Cash flows from financing activities:		
Proceeds from issuance of series B1 convertible preferred shares, net of issuance costs	57,875	—
Proceeds from issuance of series B2 convertible preferred shares, net of issuance costs	—	26,005
Proceeds from the sale of ordinary shares	1	1
Payments of initial public offering costs	—	(576)
Net cash provided by financing activities	57,876	25,430
Effect of exchange rate changes on cash	2,913	(2,449)
Net increase (decrease) in cash	58,261	(4,283)
Cash at beginning of year	9,402	67,663
Cash at end of year	$ 67,663	$ 63,380
Supplemental disclosure of cash flow information		
Cash paid for income taxes	—	73
Advance billings on deferred revenue included in accounts receivable	—	5,045
Series B2 convertible preferred financing costs accrued but not paid	—	249
Deferred initial public offering costs accrued but not paid	—	1,076

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements

1. Nature of the business and basis of presentation

Bicycle Therapeutics Limited (collectively with its subsidiaries, the "Company") is a clinical-stage biopharmaceutical company developing a novel class of medicines, which the Company refers to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic properties of a small molecule. The Company's initial internal programs are focused on oncology indications with high unmet medical need. The Company's lead product candidate, BT1718, is a *Bicycle* Toxin Conjugate ("BTC") that is being developed to target tumors that express Membrane Type 1 matrix metalloprotease. BT1718 is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial in collaboration with, and fully funded by, the Centre for Drug Development of Cancer Research UK. The Company is also developing BT5528 and BT8009, which are BTCs targeting Ephrin type-A receptor 2 and Nectin-4, respectively, for oncology indications. The Company is currently conducting Investigational New Drug application-enabling activities for BT5528 and BT8009. The Company's discovery pipeline in oncology includes *Bicycle*-targeted innate immune activators, as well as T-cell modulators. Beyond oncology, the Company is collaborating with biopharmaceutical companies and organizations in therapeutic areas that include anti-infective, cardiovascular, hematology, ophthalmology and respiratory indications.

The Company was incorporated in 2017 as a limited liability company in England and Wales to act as the holding company for three wholly-owned subsidiaries, two of which are based in the United Kingdom ("U.K.") and one of which has its principal office in Lexington, Massachusetts, near Boston. The English subsidiaries are BicycleTx Limited and BicycleRD Limited, and the U.S. subsidiary is Bicycle Therapeutics Inc.

In May 2019, the Company's board of directors and shareholders approved the reorganization of the Company's share capital by issuing ordinary shares as bonus shares to each holder of ordinary shares on the basis of 1.429 bonus shares for each ordinary share in issue (having the effect of a one for 1.429 share split (without having an impact on the nominal value of the ordinary shares)), which was effected on May 13, 2019. All issued and outstanding share and per share amounts of ordinary shares and share options included in the accompanying consolidated financial statements have been adjusted to reflect this share split for all periods presented. In addition, the number of ordinary shares that will be issued to the holders of the Company's convertible preferred shares (Note 6) and warrants to subscribe for Series A and Series B1 convertible preferred shares (Note 7) in conjunction with the closing of the IPO has been adjusted accordingly, as well as the number of ordinary shares over which options have been granted.

2017 Reorganization

Prior to December 2017, the development of *Bicycles* was conducted by Bicycle Therapeutics Limited (for the purpose of the 2017 Reorganization referred to as "BTL OldCo."), a limited liability company incorporated in England and Wales on July 13, 2009, and its wholly-owned U.S. subsidiary, Bicycle Therapeutics Inc., which was incorporated in Delaware in April 2016.

During 2017, the Company entered into a series of transactions to effect a reorganization, and created a new holding company to facilitate its ability to pursue an initial public offering ("IPO"). These transactions are collectively referred to as the 2017 Reorganization.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

1. Nature of the business and basis of presentation (Continued)

On October 27, 2017, BTL OldCo. changed its name to BicycleRD Limited. In addition, a new holding company, Bicycle Therapeutics Limited (for the purpose of 2017 Reorganization referred to as "BTL NewCo."), was incorporated as a limited liability company in England and Wales, and BicycleTx Limited was incorporated as a limited liability company in England and Wales as a wholly-owned subsidiary of BTL NewCo.

On December 4, 2017, a share-for-share exchange was enacted pursuant to which the shareholders of BTL OldCo. exchanged their shares for equivalent shares of BTL NewCo. (both in terms of share class and number). As a result, the BTL NewCo. became the sole shareholder of BTL OldCo. In addition, the holders of warrants and/or share options to subscribe for shares in BTL OldCo. terminated or surrendered their warrants and/or share options in BTL OldCo. and were issued with warrants and share options on the same terms to subscribe for equivalent shares in BTL NewCo. (both in terms of share class and number). Those holders of restricted shares in BTL OldCo. pursuant to share vesting agreements terminated their existing share vesting agreements with BTL OldCo. and entered into share vesting agreements on the same terms and in respect of equivalent shares with BTL NewCo. (both in terms of share class and number).

On December 5, 2017, BTL OldCo. transferred the entire issued share capital in Bicycle Therapeutics Inc. to BTL NewCo. and certain of its assets, including all employees, were transferred to BicycleTx Limited.

The 2017 Reorganization was accounted for as a transaction of entities under common control. Upon completion of the 2017 Reorganization, the historical consolidated financial statements of BTL OldCo. became the historical consolidated financial statements of the Company, which had nominal assets and liabilities and had not conducted any operations other than the actions incidental to the share exchange and its incorporation. The Company concluded that the reorganization resulted in no change in the material rights and preferences of each respective class of equity interests and no change in the fair value of each respective class of equity interests before and after the reorganization.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel and collaboration partners, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations, and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. Even if the Company's research and development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Liquidity

The accompanying consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Through December 31, 2018, the Company has funded its operations with proceeds from sales of convertible preferred shares (Note 6) and proceeds received

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

1. Nature of the business and basis of presentation (Continued)

from its collaboration arrangements (Note 10). Since inception, the Company has incurred recurring losses, including net losses of $16.3 million for the year ended December 31, 2017 (restated) and $21.8 million for the year ended December 31, 2018. As of December 31, 2018, the Company had an accumulated deficit of $69.9 million. The Company expects to continue to generate operating losses in the foreseeable future.

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements — Going Concern,* the Company has evaluated whether there are certain conditions and events, considered in the aggregate, that raise substantial doubt and the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. As of March 22, 2019, the issuance date of the annual consolidated financial statements for the year ended December 31, 2018, the Company expects that its cash, will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the issuance date of the annual consolidated financial statements and the interim consolidated financial statements.

The Company is seeking to complete an initial public offering ("IPO") of its ordinary shares in the form of American Depositary Shares. Upon the completion of a public offering with at least £50.0 million of gross proceeds and at a price of at least £31.10 per share, subject to appropriate adjustment in the event of any share split or other similar recapitalization (a "Qualified IPO"), the Company's outstanding convertible preferred shares will automatically convert into ordinary shares (Note 6).

In the event the Company does not complete an IPO, the Company expects to seek additional funding through private equity financings, collaborations, government grants, strategic alliances and or licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborations. The terms of any future financing may adversely affect the rights or interests of the Company's shareholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects.

Although management continues to pursue these plans, there can be no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Restatement of previously reported financial statements

In connection with the December 31, 2018 year-end financial statement close process, the Company identified misstatements in the historical consolidated financial statements, related to the fair value determination of (i) the warrant liability (Note 7) and (ii) ordinary shares utilized to calculate share based compensation expense. The fair value of the warrant liability and ordinary shares, which was derived from an independent third-party valuation report, included an error in an input to the valuation model related to the payment that would be made to the Series A and Series B1 preferred warrants holders in a sale liquidity event, following the exercise of the warrants.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

1. Nature of the business and basis of presentation (Continued)

The Company has corrected the misstatement by reflecting the impact of the revised valuation on the fair value of ordinary shares and the warrant liability for the periods that the warrants were outstanding which impacts all of the following:

- the fair value allocation between the Series B1 convertible preferred shares carrying amount and warrant liability on the date of issuance;
- the measurement of Series A convertible preferred share warrants recorded as research and development expense on issuance;
- the impact to the change in fair value of the warrant liability recorded as other expense;
- the impact of exchange rates on the translation of the warrant liability to USD included in accumulated other comprehensive income (loss);
- the impact of the revised valuation to share based compensation expense recorded as research and development and general and administrative expenses and additional paid-in capital; and
- the associated benefit from income taxes and respective deferred tax assets as recorded as other assets.

As a result, the Company has restated its consolidated balance sheet as of December 31, 2017, the related consolidated statement of operations and comprehensive loss, consolidated statement of convertible preferred shares and shareholders' (deficit) equity, and consolidated statement of cash flows for the year ended December 31, 2017. The impact of these adjustments is detailed in the tables below.

Consolidated Balance Sheet

	Previously reported		As restated
	December 31, 2017	Adjustment	December 31, 2017
		(in thousands)	
Other assets	$ 1,058	$ 69	$ 1,127
Total assets	73,932	69	74,001
Warrant liability	10,497	(6,086)	4,411
Total liabilities	30,830	(6,086)	24,744
Series B1 convertible preferred shares	49,328	5,293	54,621
Additional paid-in capital	776	62	838
Accumulated other comprehensive income (loss)	(165)	234	69
Accumulated deficit	(48,661)	565	(48,096)
Total shareholders' (deficit) equity	(48,046)	862	(47,184)

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

1. Nature of the business and basis of presentation (Continued)

Consolidated Statement of Operations and Comprehensive Loss

	Previously reported		As restated
	Year Ended December 31, 2017	Adjustment	Year Ended December 31, 2017
	(in thousands, except per share data)		
Research and development	$ 12,242	$ (376)	$ 11,866
General and administrative	6,346	61	6,407
Total operating expenses	18,588	(315)	18,273
Loss from operations	(16,528)	315	(16,213)
Other expense	(300)	181	(119)
Total other expense, net	(250)	181	(69)
Net loss before income tax provision	(16,778)	496	(16,282)
Provision for (benefit from) income taxes	46	(69)	(23)
Net loss	(16,824)	565	(16,259)
Net loss attributable to ordinary shareholders	(16,824)	565	(16,259)
Net loss per share attributable to ordinary shareholders, basic and diluted	(50.50)	1.69	(48.81)
Foreign currency translation adjustment	2,121	234	2,355
Total comprehensive loss	(14,703)	799	(13,904)

Consolidated Statement of Cash flows

	Previously reported		As restated
	Year Ended December 31, 2017	Adjustment	Year Ended December 31, 2017
		(in thousands)	
Cash flows from operating activities:			
Net loss	$ (16,824)	$ 565	$ (16,259)
Share-based compensation expense	452	63	515
Non-cash research and development expense	1,234	(378)	856
Change in fair value of warrant liability	300	(181)	119
Other assets	(970)	(69)	(1,039)

Basis of presentation

The accompanying consolidated financial statements include the accounts of Bicycle Therapeutics Limited and its wholly owned subsidiaries, BicycleTx Limited, BicycleRD Limited and Bicycle Therapeutics Inc. All intercompany balances and transactions have been eliminated on consolidation.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

1. Nature of the business and basis of presentation (Continued)

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP").

2. Summary of Significant Accounting Policies

Use of estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses, revenue recognition, the fair value of ordinary shares and share based compensation, the valuation of the warrant liability, and income taxes. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. Estimates are periodically reviewed in light of reasonable changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates or assumptions.

The Company utilizes significant estimates and assumptions in determining the fair value of its ordinary shares. The Company has utilized various valuation methodologies in accordance with the framework of the 2004 American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its ordinary shares. Each valuation methodology includes estimates and assumptions that require the exercise of judgment by the Company. These estimates and assumptions include a number of objective and subjective factors, including external market conditions, the prices at which the Company sold convertible preferred shares, the superior rights and preferences of securities senior to the Company's ordinary shares at the time of, and the likelihood of, achieving a liquidity event, such as an initial public offering or sale. Significant changes to the key assumptions used in the valuations could result in different fair values of the Company's ordinary shares at each valuation date.

Unaudited pro forma information

On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will be extinguished (Note 7).

In the accompanying consolidated statements of operations and comprehensive loss, the unaudited pro forma basic and diluted net loss per share attributable to ordinary shareholders for the year ended December 31, 2018 have been prepared to give effect, upon the closing of a Qualified IPO, to (i) the automatic conversion of all outstanding shares of convertible preferred shares into ordinary shares, and (ii) the exercise of 200,000 warrants to subscribe for Series A convertible preferred shares immediately prior to an IPO, and (iii) the exercise of the warrants to subscribe for 371,645 Series B1 convertible preferred shares which would otherwise expire upon the completion of an IPO, as if the proposed IPO had occurred on the later of January 1, 2018 or the issuance date of the convertible preferred shares or preferred share warrants.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Foreign currency and currency translation

The functional currency of Bicycle Therapeutics Limited and its wholly owned non-U.S. subsidiaries, BicycleTx Limited and BicycleRD Limited, is the British Pound Sterling and the consolidated financial statements are presented in United States dollars ("USD"). The functional currency of Bicycle Therapeutics Inc. is the USD. The functional currency is the currency of the primary economic environment in which an entity's operations are conducted. The functional currency of the Company's subsidiaries is the same as the local currency.

Monetary assets and liabilities denominated in currencies other than the functional currency are remeasured into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are remeasured into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net loss for the respective periods. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in general and administrative expense in the consolidated statements of operations and comprehensive loss as incurred. The Company recorded a foreign exchange loss of $0.6 million and a foreign exchange gain of $0.3 million for the years ended December 31, 2017 and 2018, respectively.

The Company translates the assets and liabilities of Bicycle Therapeutics Limited, BicycleTx Limited and BicycleRD Limited into USD at the exchange rate in effect on the balance sheet date. Revenues and expenses are translated at the average exchange rate in effect during the period. Unrealized translation gains and losses are recorded as a cumulative translation adjustment, which is included in the consolidated statements of convertible preferred shares and shareholders' (deficit) equity as a component of accumulated other comprehensive income (loss).

Concentrations of credit risk and of significant suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and accounts receivable. The Company deposits its cash in financial institutions in amounts that may exceed federally insured limits and has not experienced any losses on such accounts. The Company does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Accounts receivable primarily consist of amounts due under the collaboration agreements between BicycleTx Limited and AstraZeneca AB ("AstraZeneca") and Bioverativ, Inc. ("Bioverativ") and between BicycleRD Limited and Oxurion NV. ("Oxurion"), formerly ThromboGenics NV. (Note 10), for which the Company does not obtain collateral. As of December 31, 2017 and 2018, all of the Company's revenue to date has been generated from the collaboration agreements with AstraZeneca, Bioverativ, and Oxurion.

The Company relies, and expects to continue to rely, on a small number of vendors to manufacture supplies and raw materials for its development programs. These programs could be adversely affected by a significant interruption in these manufacturing services or the availability of raw materials.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Cash and cash equivalents

The Company considers all highly liquid investments with original maturities of three months or less at date of purchase to be cash equivalents. The Company had no cash equivalents at December 31, 2017 and 2018.

Accounts receivable

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices. To date, the Company has not had any write-offs of bad debt, and the Company did not have an allowance for doubtful accounts as of December 31, 2017 and 2018.

Deferred offering costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in shareholders' (deficit) equity as a reduction of proceeds generated as a result of the offering. Should an in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations and comprehensive loss. At December 31, 2018, the Company capitalized $1.6 million of offering costs, which are recorded within other assets in the consolidated balance sheets.

Property and equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful lives of the respective assets as follows:

	Estimated Useful Life
Laboratory equipment	3 to 5 years
Leasehold improvements	Lesser of lease term or useful life
Computer equipment	3 years
Furniture and office equipment	5 years

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated in accordance with the above guidelines once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. As of December 31, 2017 and 2018, there have been no significant asset retirements to date. Expenditures for repairs and maintenance are charged to expense as incurred.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Impairment of long-lived assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

Deferred rent

The Company recognizes rent expense on a straight-line basis over the respective lease terms and has recorded deferred rent for rent expense incurred but not yet paid.

Fair value measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted prices in active markets for identical assets or liabilities.
- Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 — Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's warrant liability is carried at fair value, determined according to the fair value hierarchy described above (Note 3). The carrying values of accounts receivable, research and development incentives receivable, other current assets, accounts payable and accrued expenses and other current liabilities approximate their fair values due to the short-term nature of these assets and liabilities.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Warrant liability

The Company classifies warrants to subscribe for Series A and Series B1 convertible preferred shares (Note 6) as a liability on its consolidated balance sheets as these warrants to subscribe for Series A and Series B1 convertible preferred shares are free-standing financial instruments that may require the Company to transfer assets upon exercise. The warrant liability was initially recorded at fair value upon the date of the warrants' issuance and is subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant liability are recognized as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss. Changes in the fair value of the warrant liability will continue to be recognized until the warrants to subscribe for Series A and Series B1 convertible preferred shares are exercised or expire.

Segment and geographic information

Operating segments are defined as components of a business for which separate discrete financial information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and assess performance. The Company and its chief operating decision maker, the Company's Chief Executive Officer, view the Company's operations and manages its business as a single operating segment, which is developing a unique class of chemically synthesized medicines based on its proprietary constrained peptides.

The Company operates in two geographic regions: the United Kingdom and the United States.

Revenue recognition

The Company's revenues are generated primarily through collaborative arrangements and license agreements with pharmaceutical companies. The terms of these arrangements may include (i) performing research and development services using the Company's bicyclic peptide screening platform with the goal of identifying compounds for further development and commercialization, (ii) options to obtain additional research and development services or licenses for additional targets, or to optimize product candidates, upon the payment of option fees, or (iii) the transfer of intellectual property rights (licenses).

The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, upfront license fees; payments for research and development services; fees upon the exercise of options to obtain additional services or licenses; payments based upon the achievement of defined collaboration objectives; future regulatory and sales-based milestone payments; and royalties on net sales of future products.

The Company has adopted ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606) ("ASC 606") and all subsequent amendments using the full retrospective transition method for all periods presented. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, it performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when, or as, the Company satisfies the performance obligations. The Company only applies the five-step model to contracts when it is probable that the entity will collect substantially all of the consideration it is entitled to in exchange for the goods or services it transfers to the customer. As part of the accounting for these arrangements, the Company must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Once a contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within the contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations.

Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. The promised goods or services in the Company's contracts with customers primarily consist of license rights to the Company's intellectual property for research and development, research and development services, options to acquire additional research and development services, and options to obtain additional licenses, such as a commercialization license for a potential product candidate. Promised goods or services are considered distinct when: (i) the customer can benefit from the good or service on its own or together with other readily available resources, and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own and whether the required expertise is readily available. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises.

The Company estimates the transaction price based on the amount of consideration the Company expects to receive for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of the potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected value method to estimate variable consideration to include in the transaction price based on which method better predicts the amount of consideration expected to be received. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

After the transaction price is determined it is allocated to the identified performance obligations based on the estimated standalone selling price. The Company must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction, probabilities of technical and regulatory success and the estimated costs. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amounts the Company would expect to receive for each performance obligation.

The Company then recognizes as revenue in the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time based on the use of an input method.

Licenses of intellectual property: If a license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are combined with other promises, such as research and development services and a research license, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

Research and Development Services: The promises under the Company's collaboration agreements may include research and development services to be performed by the Company on behalf of the partner. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts.

Customer Options: The Company evaluates the customer options to obtain additional items (i.e. additional license rights) for material rights, or options to acquire additional goods or services for free or at a discount. Optional future services that reflect their standalone selling prices do not provide the customer with a material right and, therefore, are not considered performance obligations and are accounted for as separate contracts. If optional future services include a material right, they are accounted for as performance obligations. The Company determines an estimated standalone selling price of any material rights for the purpose of allocating the transaction price. The Company considers factors such as the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Milestone payments: The Company's collaboration agreements may include development and regulatory milestones. The Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue and net loss in the period of adjustment.

Royalties: For sales-based royalties, including milestone payments based on the level of sales, the Company determines whether the sole or predominant item to which the royalties relate is a license. When the license is the sole or predominant item to which the sales-based royalty relates, the Company recognizes revenue at the later of: (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any sales-based royalty revenue resulting from the Company's collaboration agreements.

The Company receives payments from customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional, such as when the Company has a contractual right to payment per the terms of the contract.

For a complete discussion of accounting for collaboration revenues, see Note 10, "Significant Agreements"

Research and development costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, share-based compensation and benefits, travel, facilities costs, materials and laboratory supplies, and external costs of outside vendors engaged to conduct preclinical development, clinical development activities, as well as to manufacture clinical trial materials. Facilities costs primarily include the allocation of rent, utilities, and depreciation.

Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized until the related goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Research and manufacturing contract costs and accruals

The Company has entered into various research and development and manufacturing contracts, including contracts with respect to preclinical studies and clinical trials, with companies both inside and outside of the United States. These agreements are generally cancelable with 90 days or less notice, and related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the research and development and manufacturing activities, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Research and development incentives and receivable

The Company, through its subsidiaries in the United Kingdom, receives reimbursements of certain research and development expenditures as part of a United Kingdom government's research and development tax reliefs program. Under the program, the Company is able to surrender trading losses that arise from qualifying research and development expenses incurred by the Company's subsidiaries in the United Kingdom for a tax credit of up to 14.5% of the surrendable losses.

Management has assessed the Company's research and development activities and expenditures to determine which activities and expenditures are likely to be eligible under the research and development incentive program described above. At each period end, management estimates the reimbursement available to the Company based on available information at the time.

The Company recognizes income from the research and development incentives when the relevant expenditure has been incurred, the associated conditions have been satisfied and there is reasonable assurance that the reimbursement will be received. The Company records these research and development incentives as a reduction to research and development expenses in the statements of operations and comprehensive loss, as the research and development tax credits are not dependent on us generating future taxable income, the Company's ongoing tax status, or tax position. The research and development incentives receivable represent an amount due in connection with the above program. The Company recorded a reduction to research and development expense of $2.9 million and $5.9 million during the years ended December 31, 2017 and 2018, respectively.

Patent costs

All patent-related costs incurred in connection with preparing, filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Share-based compensation

The Company measures all equity awards granted to employees and directors based on the fair value on the date of grant. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. The Company records the expense for awards with only service-based vesting conditions using the straight-line method. The Company accounts for forfeitures as they occur.

The Company has granted awards with both a service condition that vest over time and a performance condition that will accelerate vesting upon the achievement of a specified collaboration revenue threshold. For equity awards that contain both performance and service conditions, the Company recognizes share-based compensation expense using an accelerated attribution model over the requisite service period when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance condition as of the reporting date.

For share-based awards granted to non-employee consultants, compensation expense is recognized over the period during which services are rendered by such consultants until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of the Company's ordinary shares and updated assumption inputs in the Black-Scholes option-pricing model, as applicable.

The fair value of each restricted ordinary share award is based on the fair value of the Company's ordinary shares, less any applicable purchase price. The fair value of each share option is estimated using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the fair value of ordinary shares, the expected share price volatility, the expected term of the award, the risk-free interest rate, and expected dividends.

Given the absence of an active market for the Company's ordinary shares, the board of directors determined the estimated fair value of the Company's equity instruments based on input from management which utilized the most recently available independent third-party valuation, and considering a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector. The third party valuation reports performed utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its ordinary shares. Each valuation methodology includes estimates and assumptions that require judgment. These estimates and assumptions include a number of objective and subjective factors in determining the value of the Company's ordinary shares at each grant date, including the following: (1) prices paid for the Company's convertible preferred shares, which the Company had sold to outside investors in arm's-length transactions, and the rights, preferences, and privileges of the Company's convertible preferred shares and ordinary shares; (2) the Company's stage of development; (3) the fact that the grants of share-based awards involved illiquid securities in a private company; and (4) the likelihood of achieving a liquidity event for the ordinary shares underlying the share-based awards, such as an IPO or sale of the Company, given prevailing market conditions.

Expected volatility is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information was available. The historical volatility is calculated based on a period of time commensurate with the assumption used for the expected

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

term. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption. The Company uses the simplified method, under which the expected term is presumed to be the midpoint between the vesting date and the end of the contractual term. The Company utilizes this method due to the lack of historical exercise data and the plain nature of its share-based awards. The Company uses the remaining contractual term for the expected life of non-employee awards. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on ordinary shares.

The Company classifies share-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Comprehensive loss

Comprehensive loss includes net loss as well as other changes in shareholders' (deficit) equity that result from transactions and economic events other than those with shareholders. The Company recorded unrealized gains and losses related to foreign currency translation as a component of other comprehensive loss as of December 31, 2017 and 2018.

Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential loss range is probable and reasonably estimable under the provisions of the authoritative guidelines that address accounting for contingencies. The Company expenses costs as incurred in relation to such legal proceedings as general and administrative expense within the consolidated statements of operations and comprehensive loss.

Income taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that will more likely than not be realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Net loss per share

The Company follows the two-class method when computing net loss per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net loss per share for each class of ordinary and preferred securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to ordinary shareholders for the period to be allocated between ordinary and preferred securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net loss per share attributable to ordinary shareholders is computed by dividing the net loss attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding for the period. Diluted net loss attributable to ordinary shareholders is computed by adjusting net loss attributable to ordinary shareholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net loss per share attributable to ordinary shareholders is computed by dividing the diluted net loss attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding for the period, including potential dilutive ordinary shares assuming the dilutive effect of ordinary share equivalents.

The Company's convertible preferred shares contractually entitle the holders of such shares to participate in dividends but contractually do not require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such preferred securities. In periods in which the Company reports a net loss attributable to ordinary shareholders, diluted net loss per share attributable to ordinary shareholders is the same as basic net loss per share attributable to ordinary shareholders, since dilutive ordinary shares are not assumed to have been issued if their effect is anti-dilutive.

Recently adopted accounting pronouncements

In March 2016, the FASB issued ASU No. 2016-09, *Compensation — Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting ("ASU 2016-09")*. ASU 2016-09 addresses several aspects of the accounting for share-based payment transactions, including the accounting for income taxes, forfeitures, and statutory tax withholding requirements, as well as classification in the statement of cash flows. Certain of these changes are required to be applied retrospectively, while other changes are required to be applied prospectively. The Company adopted this standard for all periods presented and its adoption did not have a material impact on the Company's financial position, results of operations or cash flows.

In March 2018, the FASB issued ASU No. 2018-05, *Income Taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118* ("ASU 2018-05"). ASU 2018-05

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

amends SEC paragraphs in ASC 740 to reflect SEC Staff Accounting Bulletin (SAB) No.118. When the 2017 Tax Cuts and Jobs Act (the "Act") was signed into law, the SEC staff released SAB 118 for applying Topic 740 as it relates to the Act. SAB 118 outlines the approach companies may take if they determine that the necessary information is not available (in reasonable detail) to evaluate, compute, and prepare accounting entries to recognize the effect(s) of the Act by the time the financial statements are required to be filed. Companies may use this approach when the timely determination of some or all of the income tax effect(s) from the Act is incomplete by the due date of the financial statements. SAB 118 also prescribes disclosures that reporting entities must provide in these circumstances. The amendments to the Accounting Standards Codification ("ASC") became effective upon issuance. During the year ended December 31, 2018, the Company did not make any adjustments to the provisional amounts recorded as a result of the Act in the year ended December 31, 2017 and the Company considers the accounting related to the Act to be final.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes ("ASU 2015-17")*. ASU 2015-17 requires deferred tax liabilities and assets to be classified as non-current in the consolidated balance sheet. The Company adopted ASU 2015-17 retrospectively to all periods presented as of December 31, 2016, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2014, the FASB issued ASU No. 2014-16, *Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share Is More Akin to Debt or to Equity ("ASU 2014-16")*. The guidance requires an entity to determine the nature of the host contract by considering all stated and implied substantive terms and features of the hybrid financial instrument, weighing each term and feature on the basis of the relevant facts and circumstances (commonly referred to as the whole-instrument approach). The Company adopted ASU 2014-16 as of the required effective date of January 1, 2016 and reflected the adoption on a retrospective basis, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the consolidated statements of cash flows. The Company adopted ASU 2016-15 retrospectively to all periods presented, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash ("ASU 2016-18")*. ASU 2016-18 requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents and amounts generally described as restricted cash or restricted cash equivalents. Entities will also be required to reconcile such total to amounts on the balance sheet and disclose the nature of the restrictions. For public entities, this guidance is effective for annual reporting periods beginning after December 15, 2017 and interim periods within those fiscal years. As early adoption was permitted, the Company adopted this standard retrospectively as of January 1, 2016. The Company does not have any restricted cash, and as such the adoption of this standard had no impact on the Company's financial position, results of operations or cash flows.

In May 2017, the FASB issued ASU 2017-09, *Compensation — Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"). The amendments in ASU 2017-09

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

clarify that modification accounting is required only if the fair value, the vesting conditions, or the classification of the awards (as equity or liability) changes as a result of the changes in terms or conditions. This guidance is effective for all entities for annual reporting periods beginning after December 15, 2017 and interim periods within those fiscal years. As early adoption was permitted, the Company adopted this standard as of January 1, 2016. The adoption of this guidance had no impact on the Company's financial position, results of operations or cash flows.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"). This guidance revises existing practice related to accounting for leases under ASC Topic 840 Leases ("ASC 840"). ASU 2016-02 will require lessees to recognize most leases on their balance sheet as a right-of-use asset and a lease liability. The lease liability will be equal to the present value of lease payments and the right-of-use asset will be based on the lease liability, subject to adjustment such as for initial direct costs. For income statement purposes, the new standard retains a dual model similar to ASC 840, requiring leases to be classified as either operating or finance. For lessees, operating leases will result in straight-line expense (similar to current accounting by lessees for operating leases under ASC 840). In July 2018, the FASB issued ASU 2018-11, *Leases (Topic 842) Targeted Improvements*, which provides an additional transition method that allows entities to initially apply the new standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption without restating prior periods. The guidance is effective for annual reporting periods beginning after December 15, 2018 and interim periods within those fiscal years, and early adoption is permitted. The Company intends to adopt the requirements of the new standard via a cumulative-effect adjustment without restating prior periods. The Company is evaluating the impact that this standard has on the lease of its corporate headquarters in the U.K., the lease of its office and laboratory space in Lexington, MA, and is currently in the process of reviewing its clinical material manufacturing contracts for any embedded leases.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"). ASU 2016-13 provides for a new impairment model that requires measurement and recognition of expected credit losses for most financial assets and certain other instruments, including but not limited to accounts receivable and available for sale debt securities. ASU 2016-13 is effective for the Company for fiscal years beginning after December 15, 2019, and interim periods within those years, with early adoption permitted. The Company is currently evaluating the impact of this guidance on its consolidated financial statements and disclosures.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation — Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07") to simplify the accounting for share-based payments to non-employees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The new guidance expands the scope of ASC 718, *Compensation — Stock Compensation*, to include share-based payments granted to non-employees in exchange for goods or services used or consumed in an entity's own operations and supersedes the guidance in ASC Topic 505-50, *Equity-Based Payments to Non-Employees*. The guidance is effective for public business entities in annual periods beginning after December 15, 2018 and interim periods within those years. Early adoption is permitted. The

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Company is currently evaluating the effect of this guidance on the Company's consolidated financial statements and disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*, which modifies, removes and adds certain disclosure requirements on fair value measurements based on the FASB Concepts Statement, *Conceptual Framework for Financial Reporting — Chapter 8: Notes to Financial Statements*. The ASU is effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted. The Company is in the process of evaluating the impact of the adoption of the ASU on its consolidated financial statements and disclosures.

3. Fair value of financial assets and liabilities

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis (in thousands):

	Fair Value Measurement as of December 31, 2017 using:			
	Level 1	Level 2	Level 3 (as restated)	Total (as restated)
Liabilities:				
Warrant liability	$ —	$ —	$ 4,411	$ 4,411
	$ —	$ —	$ 4,411	$ 4,411

	Fair Value Measurement as of December 31, 2018 using:			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Warrant liability	$ —	$ —	$ 4,804	$ 4,804
	$ —	$ —	$ 4,804	$ 4,804

The warrant liability was initially recorded at fair value upon the date of the warrants' issuance and is subsequently remeasured to fair value at each reporting date (Note 7).

During the years ended December 31, 2017 and 2018, there were no transfers between levels.

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Notes to Consolidated Financial Statements (Continued)

4. Property and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2017	2018
Laboratory equipment	$ 2,415	$ 3,356
Leasehold improvements	67	75
Computer equipment	193	221
Furniture and office equipment	26	99
	2,701	3,751
Less: Accumulated depreciation and amortization	(1,339)	(1,933)
	$ 1,362	$ 1,818

Depreciation expense was $0.3 million and $0.7 million for the years ended December 31, 2017 and 2018, respectively.

5. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2017	2018
Accrued employee compensation and benefits	$ 1,045	$ 1,610
Accrued external research and development expenses	1,995	3,814
Income taxes payable	94	15
Accrued professional fees	123	1,494
Other	148	99
	$ 3,405	$ 7,032

6. Convertible preferred shares

The Company has issued Series A convertible preferred shares ("Series A Preferred Shares"), Series B1 convertible preferred shares ("Series B1 Preferred Shares"), and Series B2 convertible preferred shares ("Series B2 Preferred Shares") (collectively the "Preferred Shares").

On May 26, 2017 the Company completed the issue of 3,562,583 Series B1 Preferred Shares at a price per share of £11.2278, for gross cash proceeds of $51.9 million. In addition, on October 27, 2017, an additional unaffiliated investor subscribed for a further 384,615 Series B1 Preferred Shares at a price per share of £13, for gross cash proceeds of $6.6 million. These two transactions are collectively referred to as "the Series B1 Financing". In conjunction with the Series B1 Financing, the Company also issued warrants to subscribe for 743,287 Series B1 Preferred Shares to the subscribers of the Series B1 Preferred Shares (Note 7). The Company allocated a portion of the proceeds equal to the fair value of the warrants at the date of grant to the warrant liability, and the remaining amount was allocated to the Series B1 Preferred Shares.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

6. Convertible preferred shares (Continued)

On December 20, 2018, the Company completed the issue of 1,323,248 Series B2 preferred shares at a price per Series B2 preferred share of £15.55, for gross cash proceeds of $26.1 million (the "Series B2 Financing"). In conjunction with the Series B2 Financing, the existing holders of warrants to subscribe for Series B1 preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 preferred shares and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 preferred shares to the new investor. In conjunction with the Series B2 Financing, the Company designated all previously outstanding Series B preferred shares as Series B1 preferred shares.

The rights, preferences, and privileges of the Preferred Shares are described below:

Voting rights

The holders of Preferred Shares are entitled to vote, together with the holders of ordinary shares, on all matters submitted to shareholders for a vote, except as required by law. Each preferred shareholder is entitled to the number of votes equal to the number of ordinary shares into which each preferred share is convertible as of the date of the vote.

Liquidation preferences

In the event that the Company liquidates, dissolves or winds up, whether voluntarily or involuntarily, the Company sells all or substantially all of its assets or businesses, or the Company sells the whole or any part of the issued share capital of a subsidiary, the shareholders of the Company sell a controlling interest in the Company, or if certain events deemed to be a liquidation occur, then the holders of the Series B2 Preferred Shares are entitled to receive in preference to the holders of the Series B1 Preferred Shares, the Series A Preferred Shares and the ordinary shares an amount per share equal to the original purchase price of the Series B2 Preferred Shares, plus any dividends, if declared but unpaid thereon. In addition, following payment of the preference to the holders of Series B2 Preferred Shares, the holders of the Series B1 Preferred Shares are entitled to receive in preference to the holders of the Series A Preferred Shares and the ordinary shares an amount per share equal to the original purchase price of each respective Series B1 Preferred Share, plus any dividends, if declared but unpaid thereon. In addition, following payment of the preference to the holders of Series B1 Preferred Shares, the holders of the Series A Preferred Shares are entitled to receive in preference to the holders of the ordinary shares, an amount per share equal to the original purchase price of each respective Series A Preferred Share, plus any dividends, if declared but unpaid thereon. Following all preferential payments to holders of the Preferred Shares, as required, any remaining undistributed assets are shared ratably with the holders of the ordinary shares and the convertible preferred shares with the latter's share number being determined on an "as-if-converted" basis.

Dividends

The holders of the Preferred Shares rank pari passu in all respects as to dividends with the holders of the ordinary shares. The Company may not pay any dividends on ordinary shares of the Company unless the holders of Preferred Shares then outstanding simultaneously receive dividends at the same rate and same time as dividends paid with respect to ordinary shares. Through December 31, 2017 and 2018, no dividends have been declared or paid.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

6. Convertible preferred shares (Continued)

Redemption rights

The Preferred Shares are not redeemable at the option of the holder.

The holders of Preferred Shares have liquidation rights in the event of a deemed liquidation that, in certain situations such as a change in control, are not solely within the control of the Company. Therefore, convertible preferred shares are classified outside of shareholders' (deficit) equity.

Conversion rights

Each Preferred Share is convertible at any time at the option of the shareholder into fully paid ordinary shares. Each Preferred Share will be automatically converted into such number of ordinary shares, at the applicable conversion ratio then in effect, upon either (i) the closing of a firm commitment public offering with at least £50.0 million of gross proceeds and at a price of at least £31.10 per share, subject to appropriate adjustment in the event of any share split, share dividend, combination or other similar recapitalization, or (ii) the vote or written consent of the holders of at least a 77% of the outstanding Preferred Shares on an as converted basis, voting together as a single class.

The Preferred Shares are initially convertible to ordinary shares on a one for one basis, subject to adjustment for certain dilutive events and certain capital reorganizations in accordance with the terms of the articles of association of the Company.

Upon issuance of each class of Preferred Shares, the Company assessed the embedded conversion and liquidation features of the securities. The Company determined that each class of Preferred Shares does not require the Company to separately account for the conversion or liquidation features. The Company also concluded that no beneficial conversion features existed upon the issuance date of the Series A Preferred Shares, Series B1 Preferred Shares, or Series B2 Preferred Shares.

7. Warrant liability (restated)

On May 26, 2017, the Company issued 200,000 warrants to subscribe for Series A Preferred Shares at £0.01 each which are exercisable at any time after May 26, 2017 provided that they have not otherwise lapsed in accordance with their terms. The warrants were issued as consideration to amend a royalty arrangement (Note 12) with certain founders of the Company. The Company recorded the fair value of the warrants to subscribe for Series A Preferred Shares to the founders of $0.9 million as research and development expense at the time of issuance in May 2017, as the underlying license rights do not have alternative future use, in accordance with ASC Topic 730, Research and Development.

The warrants to subscribe for Series A Preferred Shares expire upon the earlier of (i) 10 years from their issuance date, or (ii) upon an IPO or exit unless an exercise delay notice is provided by the Series A warrant holder, in which case they will expire 12 months following an IPO or exit.

On May 26, 2017, in conjunction with the issuance of 3,562,583 Series B1 Preferred Shares at a price per share of £11.2278 (Note 6), the Company issued 627,903 warrants to subscribe for Series B1 Preferred Shares with an exercise price of £0.01. In addition, on October 27, 2017, in

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

7. Warrant liability (restated) (Continued)

conjunction with the issuance of 384,615 Series B1 Preferred Shares the Company issued a further 115,384 warrants to subscribe for Series B1 Preferred Shares with an exercise price of £0.01. In conjunction with the Series B2 Financing (Note 6), the existing holders of warrants to subscribe for Series B1 preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 preferred shares and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 preferred shares to the new investor.

The warrants to subscribe for Series B1 Preferred Shares may be exercised from the first to occur of (i) March 31, 2020, (ii) upon notification of an equity fund raise for aggregate proceeds of a minimum amount to be determined by the board of directors of the Company, (iii) the notification of initiation of an IPO, (iv) notification of an exit (being either: (a) a sale or other transfer of the whole or any part of the issued share capital of the Company or any subsidiary on an arm's length basis that results in such person (along with any persons acting in concert) holding a controlling interest in the Company or any subsidiary; or (b) the disposition of all or substantially all of the assets or business of the Company to a third party (either by way of a sale, license and/or other transfer), or (v) upon an unfavorable outcome related to a patent complaint (Note 12). The Series B1 Warrants expire upon five years from becoming exercisable, or immediately prior to an exit (having the meaning set out above in this paragraph), IPO, an equity fund raise (having the meaning set out above in this paragraph), upon a favorable judgment related to a patent complaint (Note 12), or upon the winding up of the Company. The warrants to purchase Series B1 preferred shares contain limitations on their ability to be exercised based on the status of the patent complaint, in accordance with the terms of the warrant agreement.

The warrants to subscribe for Series A and Series B1 Preferred Shares are recorded as a liability and remeasured to fair value at each reporting date (Note 3). Changes in the fair value of the warrant liability are recognized as other expense, net in the consolidated statements of operations and comprehensive loss. The following table provides a roll-forward of the fair values of the Company's warrant liability for which fair value is determined by Level 3 inputs (in thousands):

	Warrant Liability
Fair value at December 31, 2016	$ —
Issuance of warrants to subscribe for Series A convertible preferred shares (as restated)	856
Issuance of warrants to subscribe for Series B1 convertible preferred shares (as restated)	3,254
Change in fair value of warrant liability recorded as other expense (as restated)	119
Impact of exchange rates on translation of warrant liability to USD included in accumulated other comprehensive income (loss) (as restated)	182
Fair value at December 31, 2017 (as restated)	4,411
Change in fair value of warrant liability recorded as other expense	665
Impact of exchange rates on translation of warrant liability to USD included in accumulated other comprehensive income (loss)	(272)
Fair value at December 31, 2018	$ 4,804

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

7. Warrant liability (restated) (Continued)

In conjunction with the Series B2 Financing (Note 6), the existing holders of warrants to subscribe for Series B1 preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 preferred shares and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 preferred shares to the new investor. The transfer of warrants between investors did not have an impact to the valuation of the warrant liability, as this represents a transaction between shareholders and the Company did not issue any new instruments or change the rights and preferences of the underlying warrants to subscribe for Series B1 preferred shares.

The warrant liability in the table above consisted of the fair value of warrants to subscribe for Series A and Series B1 Preferred Shares (see Note 6) and was based on significant inputs not observable in the market, which represent a Level 3 measurement within the fair value hierarchy. The Company's valuation of the warrants to subscribe for Series A and Series B1 Preferred Shares utilized the Black-Scholes option-pricing model, which incorporates assumptions and estimates to value the warrant liability. The Company assesses these assumptions and estimates on a quarterly basis as additional information impacting the assumptions is obtained.

The quantitative elements associated with the Company's Level 3 inputs impacting the fair value measurement of the warrant liability include the fair value per share of the underlying Series A and Series B1 preferred shares into which the warrant is exercisable, the remaining contractual term of the warrants, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying convertible preferred shares.

The most significant assumption in the Black-Scholes option-pricing model impacting the fair value of the warrant liability is the fair value of the Series A and Series B1 preferred shares into which the warrant is exercisable as of each remeasurement date. Given the absence of an active market for the Company's equity securities, Company determines the fair value per share of the convertible preferred shares underlying the warrants by taking into consideration the implied value derived from an independent third-party valuation of the Company's ordinary shares (Note 1), adjusted for certain restrictions on the exercise of the B1 warrants per their contractual terms. Assumptions related to the remaining term, free interest rate, expected dividend yield and expected volatility do not have an impact to the fair value of the warrants because the exercise price of the warrants is £0.01, and the fair value of the warrant is equal to the difference between the exercise price and the fair value regardless of the assumptions. The Company historically has been a private company and lacks company-specific historical and implied volatility information of its shares. Therefore, it estimates its expected share volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrants. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrants. The Company has estimated a 0% dividend yield based on the expected dividend yield and the fact that the Company has never

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

7. Warrant liability (restated) (Continued)

paid or declared dividends. The following table presents the unobservable inputs to the fair value measurement of the warrant liability:

	December 31, 2017		December 31, 2018	
	Series A Warrants	Series B1 Warrants	Series A Warrants	Series B1 Warrants[1]
Risk free rate	2.4%	2.3%	2.6%	2.5%
Expected dividend yield	—%	—%	—%	—%
Expected term (years)	9.4	7.25	8.4	6.25
Expected volatility	71.4%	70.5%	75.4%	79.6%
Exercise price	£ 0.01	£ 0.01	£ 0.01	£ 0.01
Fair value preferred share underlying the warrant	$ 4.68	$ 4.68	$ 8.61	$ 4.15

(1) The fair value of the Series B1 preferred shares underlying the warrants to purchase Series B1 preferred shares at December 31, 2018 includes a 50% probability that the warrants will be not be exercisable prior to the IPO, based on their contractual terms.

In connection with the December 31, 2018 year-end financial statement close process, the Company identified misstatements in the historical consolidated financial statements, related to the fair value determination of (i) the warrant liability and (ii) ordinary shares utilized to calculate share based compensation expense. The fair value of the warrant liability and ordinary shares, which was derived from an independent third-party valuation report, included an error in an input to the valuation model related to the payment that would be made to the Series A and Series B1 warrant holders in a sale liquidity event, following their exercise. Specifically, the payment to the warrant holders in a sale liquidity event, which is one of the exit scenarios in the valuation, is equal to the purchase price paid of £0.01 for each respective share, whereas it had previously utilized the original issuance price of the Series A Preferred shares of £10, and £11.2278 and £13.00 for the Series B1 preferred shares. The Company has corrected the misstatement by recording a decrease in the warrant liability, and the related impacts on the Series B1 convertible preferred shares carrying value, share-based compensation, additional paid-in-capital, benefit from income taxes and deferred tax assets for the impact of the revised valuation on the fair value of ordinary shares and the warrant liability for the periods that the warrants were outstanding (Note 1).

On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will expire.

8. Ordinary shares

Each holder of ordinary shares is entitled to one vote per ordinary share and to receive dividends when and if such dividends are recommended by the board of directors and declared by the shareholders. As of December 31, 2017 and 2018, the Company has not declared any dividends.

As of December 31, 2017, the Company's authorized capital share capital consisted of 12,726,395 ordinary shares with a nominal value of £0.01 per share. As of December 31, 2018, the Company's authorized capital share capital consisted of 15,452,420 ordinary shares with a nominal value of £0.01 per share.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

9. Share-based compensation

Employee incentive pool

The Company is authorized to issue ordinary shares, as well as options and other securities exercisable for or convertible into ordinary shares, as incentives to its employees, consultants, and members of its board of directors. To the extent such incentives are in the form of share options, the options may have been granted pursuant to a potentially tax-favored Enterprise Management Incentive, or EMI, scheme available to U.K. employees, directors and consultants of the Company. The issuance of share options and ordinary shares is administered by the board of directors using standardized share option and share subscription agreements.

As of December 31, 2017, the Company was authorized to issue a total of 1,582,209 ordinary shares under a reserve set aside for equity awards. As of December 31, 2018, the Company was authorized to issue a total of 2,302,442 ordinary shares under a reserve set aside for equity awards. As of December 31, 2017 and 2018, there were 240,689 and 694,534 ordinary shares available for future issuance to the Company's employees, consultants and members of the board of directors. Awards of restricted ordinary shares, which are referred to as employee shares, are subject to vesting. Unvested employee shares are subject to repurchase upon termination of employment.

Options granted, as well as restricted shares granted as employee incentives, typically vest over a four-year service period with 25% of the award vesting on the first anniversary of the commencement date and the balance thereafter in 36 equal monthly instalments, and expire no later than 10 years from the date of grant.

Certain equity awards were issued in 2017 for which 20% of the award vests upon the first anniversary of the vesting start date, 60% vests thereafter in 36 equal monthly installments, and 20% vest upon the earlier of the fourth anniversary of the vesting start date, or the achievement of a specified revenue threshold from the Company's collaboration arrangements. Options granted generally expire 10 years from the date of grant.

Options issued to U.K. employees have an exercise price of £0.01 per share. The exercise price for share options granted to U.S. employees, which are not subject to the EMI schemes, have an exercise price that is not less than the fair value of ordinary shares as determined by the board of directors as of the date of grant. The Company's board of directors values the Company's ordinary shares based on input from management, considering the most recently available valuation of ordinary share performed by an independent third-party valuation firm as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

On December 17, 2018, each of the U.K. employees that were holders of share options, each with an exercise price of £0.01 per share, surrendered all of their issued share options that had not lapsed or been exercised. Thereafter, such persons: (a) subscribed for ordinary shares equal to such number of ordinary shares as were vested under their surrendered option agreement at a subscription price of £0.01 per ordinary share; and (b) were granted options to subscribe for ordinary shares equal to such number of ordinary shares as were unvested under their surrendered option agreement at a subscription price of £0.01 per ordinary share, and with identical vesting terms as the original awards. In conjunction with the surrender of 340,728 vested share options, the Company issued 340,728 ordinary shares. The Company evaluated the surrender of share options and issuance of vested ordinary shares and unvested share options as a modification in

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Notes to Consolidated Financial Statements (Continued)

9. Share-based compensation (Continued)

accordance with ASU 2017-09. The modification did not have any accounting impact as there were no changes in the fair value, vesting conditions, or the classification of the awards (as equity or liability) in conjunction with the surrender of share options and issuance of vested ordinary shares and unvested share options.

Share-based compensation

The Company recorded share-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,	
	2017 (as restated)	2018
Research and development expenses	$ 241	$ 513
General and administrative expenses	274	510
	$ 515	$ 1,023

Share options

The following table summarizes the Company's option activity since December 31, 2017:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2017 (as restated)	964,538	$ 0.70	8.95	$ 1,855
Granted	282,981	0.93		
Exercised	(9,361)	0.01		
Forfeited	(33,718)	0.76		
Surrendered of share options for subscription to vested shares	(340,728)	0.01		
Outstanding as of December 31, 2018	863,712	$ 1.01	8.75	$ 3,292
Vested and expected to vest as of December 31, 2018	863,712	$ 1.01	8.75	$ 3,292
Options exercisable as of December 31, 2018	213,103	$ 1.57	8.51	$ 693

The weighted average grant-date fair value of share options granted during the years ended December 31, 2017 (restated) and 2018 was $1.78 per share and $3.73 per share, respectively.

For the years ended December 31, 2017 and 2018, the Company recorded share-based compensation expense for share options granted of $0.4 million and $0.8 million, respectively.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

9. Share-based compensation (Continued)

Expense for non-employee consultants for the years ended December 31, 2017 and 2018, was immaterial.

The aggregate intrinsic value of share options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares. The aggregate intrinsic value of share options exercised during the years ended December 31, 2017 and 2018 was $7,000 and $23,000 respectively.

During the year ended December 31, 2017 and 2018, the Company granted options for the purchase of an aggregate of 678,610 and 70,875 ordinary shares, respectively, for which 20% of the award vests upon the first anniversary of the vesting start date, 60% vests thereafter in 36 equal monthly installments, and 20% on the earlier of the fourth anniversary of the vesting start date, or the achievement of a specified revenue threshold from the Company's collaboration arrangements. The Company concluded that the accelerated vesting condition was not probable at December 31, 2017. In May 2018, the Company determined that the performance condition became probable of achievement and recorded a cumulative catch-up to reflect the expense as if the vesting condition was probable of achievement at the time of the grant of the award. The Company recorded expense of $0.3 million and $0.7 million, during the year ended December 31, 2017 (restated) and 2018, respectively, related to these awards, which includes the acceleration of vesting expense.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the fair value of share options granted to employees and directors:

	Year Ended December 31,	
	2017	2018
Risk-free interest rate	2.0%	2.7%
Expected volatility	79.7%	78.6%
Expected dividend yield	—	—
Expected term (in years)	6.07	6.07

As of December 31, 2018, total unrecognized compensation expense related to the unvested employee and director share-based awards was $1.0 million, which is expected to be recognized over a weighted average period of 3.1 years.

Restricted shares

The Company has granted restricted shares with service-based vesting conditions. Shares of unvested restricted shares may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award. These restricted shares are subject to repurchase rights, for aggregate consideration of £1. Accordingly, the Company has recorded the proceeds from the issuance of restricted shares as a liability in the consolidated balance sheets included as a component of accrued expenses and other current liabilities. The restricted share liability is reclassified into shareholders' (deficit) equity as the restricted shares vest.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

9. Share-based compensation (Continued)

The following table summarizes the Company's restricted ordinary share award activity since December 31, 2017:

	Shares	Weighted Average Grant-Date Fair Value
Unvested restricted ordinary shares as of December 31, 2017 (as restated)	162,466	$ 1.83
Issued	28,985	4.02
Forfeited	(11,860)	1.41
Vested	(95,644)	2.46
Unvested restricted ordinary shares as of December 31, 2018	83,947	$ 1.93

For the years ended December 31, 2017 (as restated) and 2018, the Company recorded share-based compensation expense of $0.1 million and $0.2 million, respectively, for unvested restricted shares granted.

The fair value of employee restricted share awards vested during the years ended December 31, 2017 (as restated) and 2018, based on estimated fair values of the ordinary shares underlying the restricted share awards on the day of vesting, was $0.1 million and $0.2 million, respectively.

As of December 31, 2018, total unrecognized compensation cost related to the unvested employee and director restricted share awards was $0.2 million, which is expected to be recognized over a weighted average period of 1.9 years.

10. Significant Agreements

For the years ended December 31, 2017 and 2018, the Company had collaboration agreements with AstraZeneca, Bioverativ, ("Bioverativ"), and Oxurion. The following table summarizes the revenue recognized in the Company's consolidated statements of operations and comprehensive loss from these arrangements (in thousands):

	Year Ended December 31,	
	2017	2018
Collaboration revenues		
AstraZeneca	$ 890	$ 1,386
Bioverativ	355	4,007
Oxurion	815	1,743
Total collaboration revenues	$ 2,060	$ 7,136

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

AstraZeneca Collaboration Agreement

Summary of Agreement — 2016 Agreement

In November 2016, the Company entered into a Research Collaboration Agreement (the "AstraZeneca Collaboration Agreement") with AstraZeneca. The collaboration is focused on the research and development of Bicycle peptides that bind to up to six biological targets. After discovery and initial optimization of such Bicycle peptides, AstraZeneca will be responsible for all research and development, including lead optimization and drug candidate selection. AstraZeneca has option rights, at drug candidate selection, which allow it to obtain development and exploitation license rights with regard to such drug candidate. The initial research obligation focuses on two targets within respiratory, cardiovascular and metabolic disease. AstraZeneca also has an option to nominate up to four additional targets at any point up to the second anniversary of the agreement ("Additional Four Target Option"). The exercise of this option right results in an option fee payable to the Company of $5.0 million and the research obligations and rights are consistent with the obligations and rights related to the initial two targets discussed below.

Under the AstraZeneca Collaboration Agreement, the Company is obligated to use commercially reasonable efforts to perform research activities on the initial two targets, under mutually agreed upon research plans. The research plans includes two discrete parts, on a research program by research program basis: (i) the Bicycle Research Term, which is focused on the generation of Bicycle peptide libraries using the Company's peptide drug discovery platform, to be screened against selected biological targets and optimization of promising compounds, with the goal of identifying compounds that meet the criteria set by the parties, and (ii) the AZ Research Term, during which AstraZeneca may select certain compounds and continue research activities on those compounds, at its sole expense, with the goal of identifying compounds that satisfy the relevant pharmacological and pharmaceutical criteria for clinical testing. AstraZeneca may, at its sole discretion, approve any compound to be progressed into drug development and, upon the selection of each drug candidate, AstraZeneca is to pay $8.0 million as an option fee, in order to obtain worldwide development and exploitation rights.

Each research program is to continue for an initial period of three years (the "Research Term"), including one year for the Bicycle Research Term and two for the AZ Research Term. AstraZeneca may extend the Research Term for each research program by twelve months (or fifteen months, if needed to complete certain toxicology studies). The Research Term for a specific program can be shorter if it is ceased due to a screening failure, a futility determination, abandonment by AstraZeneca, or upon selection of a drug candidate. AstraZeneca has certain substitution rights should a screening failure or futility determination be reached but is obligated to fund these additional efforts related to substitution.

Under the terms of the AstraZeneca Collaboration Agreement, the Company granted to AstraZeneca, for each research program, a right and license (with the right to sublicense) certain background and platform intellectual property, for the duration of the applicable Research Term, to the extent necessary or useful for AstraZeneca to conduct the activities assigned to it in the applicable research plan, but for no other purpose.

The activities under the AstraZeneca Collaboration Agreement are governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

AstraZeneca. The JSC oversees and reviews each research program. Among other responsibilities, the JSC monitors and reports on research progress and ensure open and frequent exchange between the parties regarding research program activities.

AstraZeneca is obligated to fund two full time equivalents ("FTE") during the Bicycle Research Term, for each research program, based on an agreed upon FTE reimbursement rate. Payment is made quarterly in advance of services being provided.

AstraZeneca has the option to obtain development and commercialization licenses associated with each designated drug candidate in return for a fee of $8.0 million per drug candidate. In addition, AstraZeneca is required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial milestones. More specifically, for each research program, the Company is eligible to receive up to $29.0 million in development milestone payments and up to $23.0 million in regulatory milestone payments. The Company is also eligible for up to $110.0 million in commercial milestone payments, on a research program by research program basis. Development milestone payments are triggered upon initiation of a defined phase of clinical research for a drug candidate. Regulatory milestone payments are triggered upon approval to market a product candidate by the United States Food and Drug Administration ("FDA") or other global regulatory authorities. Commercial milestone payments are triggered when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. In addition, to the extent any of the product candidates covered by the licenses conveyed to AstraZeneca are commercialized, the Company would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including in certain countries where AstraZeneca faces generic competition. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from AstraZeneca.

Either party may terminate the AstraZeneca Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. Either party may terminate the AstraZeneca Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. AstraZeneca may terminate the AstraZeneca Collaboration Agreement, entirely or on a licensed product by licensed product or country by country basis, for convenience.

Accounting Analysis

The Company has identified the following performance obligations:

(i) research license and the related research and development services during the Bicycle Research Term for the first target (the "Target One Research License and Related Services"),

(ii) research license and the related research and development services during the Bicycle Research Term for the second target (the "Target Two Research License and Related Services").

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

The Company concluded that the Additional Four Target Option is not a material right, as the option does not provide a discount that AstraZeneca otherwise would not have received. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract. The Company has concluded that the research license is not distinct from the research and development services during the Bicycle Research Term as AstraZeneca cannot obtain the benefit of the research license without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as it relates to constrained peptide technology that is not available in the marketplace. As a result, for each research program, the research license has been combined with the research and development services into a single performance obligation.

The total transaction price was initially determined to be $1.2 million, consisting solely of research and development funding. The Company utilizes the most likely amount method to determine the amount of research and development funding to be received. Additional consideration to be paid to the Company upon the exercise of the license options by AstraZeneca or upon reaching certain milestones is excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the option exercise or are outside of the initial contact term.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the Target One and Target Two Research License and Related Services is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin what would be expected to be realized under similar contracts. The transaction price allocated to each performance obligation was initially $0.6 million.

The Company will recognize revenue related to amounts allocated to the Research License and Related Services as the underlying services are performed over the one year Research Term using a proportional performance model over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent time expected and will remeasure its progress towards completion at the end of each reporting period, which best reflects the progress towards satisfaction of the performance obligation.

In October 2017, AstraZeneca selected a replacement target for the first target, and as such a new Research Term was started related to the Target One Research License and Related Services. In addition, both programs were extended. The total transaction price under the arrangement increased to $1.9 million for the additional research and development funding to be received.

For the years ended December 31, 2017 and 2018, the Company recognized $0.9 million and $1.0 million, respectively, of collaboration revenue related to the Target One and Target Two Research License and Related Services for its Collaboration Agreement with AstraZeneca. As of December 31, 2017 and 2018, the Company recorded no deferred revenue and $8,000 of deferred revenue, respectively, in connection with the 2016 AstraZeneca Collaboration Agreement.

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

May 2018 AstraZeneca Option Exercise — Additional Four Targets

Under the AstraZeneca Collaboration Agreement, AstraZeneca was granted an option to nominate up to four additional targets at any point up to the second anniversary of the agreement ("Additional Four Target Option"). In May 2018, AstraZeneca made an irrevocable election to exercise the Additional Four Target Option. As a result, AstraZeneca is entitled to obtain research and development services with respect to Bicycle peptides that bind to up to four additional targets, along with license rights to those selected targets, in exchange for an option fee of $5.0 million to be paid by AstraZeneca to the Company no later than January 31, 2019. AstraZeneca is obligated to fund two FTEs during the Bicycle Research Term, for each research program, based on an agreed upon FTE reimbursement rate. Payment is made quarterly in advance of services being provided. AstraZeneca has the option to obtain worldwide development and commercialization licenses associated with each designated drug candidate in return for a fee of $8.0 million per drug candidate, upon the selection of such drug candidate, after which AstraZeneca would be required to fund development and commercialization costs, and to pay regulatory and commercial milestone payments and royalties to BicycleTX as for the other products developed under the AstraZeneca Collaboration Agreement.

Accounting Analysis

Upon the execution of the agreement, the Company has identified the following five performance obligations associated with the AstraZeneca May 2018 Agreement:

(i) Research license and the related research and development services during the Bicycle Research Term for the third target (the "Target Three Research License and Related Services"),

(ii) Material right associated with the development and exploitation license option for the third target ("Target Three Material Right"),

(iii) Material right associated with the research services option, including the underlying development and exploitation license option for the fourth target ("Target Four Material Right"),

(iv) Material right associated with the research services option, including the underlying development and exploitation license option for the fifth target ("Target Five Material Right"), and

(v) Material right associated with the research services option, including the underlying development and exploitation license option for the sixth target ("Target Six Material Right").

The Company concluded that the fourth, fifth and sixth targets available for selection are options. Upon exercise, AstraZeneca will obtain a research license and the related research and development services and an option to a development and exploitation license. The Company has concluded that the research services option, including the underlying development and exploitation license options related to each respective target results in a material right as the option exercise fee related to the development and exploitation license contains a discount that AstraZeneca would not have otherwise received.

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

The research license and the related research and development services related to the fourth, fifth and sixth targets are not performance obligations, as they are optional services that will be performed if AstraZeneca selects additional targets and they reflect their standalone selling prices and do not provide the customer with material rights. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract.

The total transaction price was determined to be $5.7 million, consisting of the $5.0 million option exercise fee and research and development funding of an estimated $0.7 million. The research and development funding is being provided based on the costs that are incurred to conduct the research and development services. The Company utilizes the most likely amount method to determine the amount of research and development funding to be received. Additional consideration to be paid to the Company upon the exercise of the license options by AstraZeneca or upon reaching certain milestones are excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the license option exercise or are outside of the initial contact term.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for each Research License and Related Services obligation is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin what would be expected to be realized under similar contracts. The estimated standalone selling price for the material rights was determined based on the fees AstraZeneca would pay to exercise the license options, the estimated value of the License Option using comparable transactions, and the probability that (i) AstraZeneca would opt into the target development, and (ii) the license options would be exercised by AstraZeneca. Based on the relative standalone selling price, the allocation of the transaction price to the separate performance obligations is as follows (in thousands):

Performance Obligations	Allocation of Transaction Price
Target Three Research License and Related Services	$ 650
Target 3 Material Right	1,504
Target 4 Material Right	1,204
Target 5 Material Right	1,165
Target 6 Material Right	1,127
	$ 5,650

The Company will recognize revenue related to amounts allocated to the Target Three Research License and Related Services as the underlying services are performed using a proportional performance model over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent time expected, which best reflects the progress towards satisfaction of the performance obligation. The amount allocated to the material rights is recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the option.

For the year ended December 31, 2018, the Company recognized $0.4 million of revenue related to the Target Three Research License and Related Service related to the May 2018

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

AstraZeneca Option Exercise. As of December 31, 2018, the Company recorded $4.7 million of deferred revenue in connection with the AstraZeneca Collaboration.

Bioverativ Collaboration Agreement

Summary of Agreement

In August 2017, the Company entered into a Collaboration Agreement (the "Bioverativ Collaboration Agreement") with Bioverativ. Under the Bioverativ Collaboration Agreement the Company will provide for research and development services focused on up to three collaboration programs; (i) Sickle cell disease, (ii) Hemophilia, and (iii) and a third program ("Program 3"), which is an optional program, to be defined. The Company will use its bicyclic peptide screening platform to perform research and development services for the programs and Bioverativ has the ability to select a collaboration product for each program and obtain a license to develop and exploit the selected collaboration product for an additional option fee.

Under the Bioverativ Collaboration Agreement, the Company is obligated to perform research activities on the initial two named collaboration programs, under mutually agreed upon research plans. The research and development services for each program consist of two stages. The first is an initial stage of screening for high affinity binders and affinity maturation of such binders to identify lead compounds led by the Company (the "BV Bicycle Research Term"). Upon the conclusion of the BV Bicycle Research Term, Bioverativ can, at is sole discretion, select a certain number of collaboration compounds to move forward into the Joint Research Term. Upon selection of the collaboration compounds, Bioverativ is required to pay an option fee. During the Joint Research Term, the Company and Bioverativ will jointly conduct research and development activities which will include lead optimization of lead compounds, in preparation for lead collaboration product nomination ("Joint Research Term"). Bioverativ may, at its sole discretion, approve any compound to be progressed into drug development and upon the selection of each collaboration product candidate, Bioverativ shall pay $5.0 million as an option fee, in order to obtain worldwide development and exploitation rights for that collaboration product.

Each research program shall continue for an initial period of three years (the "Research Term") unless a program is abandoned by Bioverativ or extended for up to one year. The first year of each Research Term shall be the BV Bicycle Research Term and the remaining part of the Research Term, including any extensions of the Research Term, shall be the Joint Research Term.

Under the terms of the Bioverativ Collaboration Agreement, the Company granted to Bioverativ, for each collaboration program, a non-exclusive, sublicensable (through multiple tiers), worldwide license under certain intellectual property of the Company to conduct the activities assigned to Bioverativ in the applicable research plan for the duration of the applicable Research Term, but for no other purpose.

The activities under the Bioverativ Collaboration Agreement will be governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and Bioverativ. The JSC will oversee, review and recommend direction of each collaboration program and variations of or modifications to the research plans.

Under the terms of the Bioverativ Collaboration Agreement, the Company received a $10.0 million up-front cash payment. Additionally, prior to the initiation of the research plan for each

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

collaboration program, Bioverativ made a non-refundable payment of $1.4 million for the Sickle cell program and $2.8 million for the Hemophilia program as payment for the Company's services during the BV Bicycle Research Term. During the Joint Research Term, Bioverativ is obligated to fund a minimum of two FTE's based on an agreed upon FTE reimbursement rate and fund certain external costs incurred by the Company. Bioverativ has the option to obtain development and commercialization licenses associated with each designated collaboration product candidate in return for a fee of $5.0 million per drug candidate. In addition, Bioverativ would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, for each collaboration program, the Company is eligible to receive between $47.5 million and $67.0 million in development milestone payments for the Sickle Cell and Hemophilia programs, respectively, and up to $104.0 million in regulatory milestone payments for each program. In addition, the Company is eligible for up to $55.0 million in commercial milestone payments, on a research program by research program basis. Development milestone payments are triggered upon initiation of a defined phase of clinical research for a collaboration product. Regulatory milestone payments are triggered upon approval to market a product candidate by the FDA or other global regulatory authorities. Commercial milestone payments are triggered when an approved collaboration product reaches certain defined levels of net sales by the licensee. In addition, to the extent any of the collaboration products covered by the licenses conveyed to Bioverativ are commercialized, the Company would be entitled to receive tiered royalty payments of mid-single digits to low double digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including for instances where Bioverativ faces generic competition in certain countries. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from Bioverativ.

Under the terms of the Collaboration Agreement, Bioverativ was also provided with an option to obtain screening services on the additional Program 3 target upon making an option fee payment of $5.0 million in addition to a non-refundable payment of $1.4 million as payment for the Company's services related to Program 3 during the BV Bicycle Research Term. The option expired in November 2018 unexercised.

Either party may terminate the Bioverativ Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. Either party may terminate the Bioverativ Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. Bioverativ may terminate the Bioverativ Collaboration Agreement, entirely or on a program by program, licensed product by licensed product or country by country basis, for convenience upon not less than 30 days prior written notice to the Company.

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

Accounting Analysis

The Company has identified the following four performance obligations associated with the Bioverativ Collaboration Agreement:

(i) Research License and the related research and development services during the BV Bicycle Research Term for Sickle cell program (the "Sickle Cell Research License and Related Services"),

(ii) Research License and the related research and development services during the BV Bicycle Research Term for Hemophilia program (the "Hemophilia Research License and Related Services"),

(iii) Material right associated with the sickle cell program development and exploitation license option ("Sickle Cell License Option Material Right"), and

(iv) Material right associated with the hemophilia program development and exploitation license option ("Hemophilia License Option Material Right").

The Company concluded that the option to obtain screening services on the additional Program 3 target is not a material right, as the option does not provide a discount that Bioverativ otherwise would not have received. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract. Research license and the related research and development services related to the Joint Research Term are not performance obligations at the inception of the arrangement, as they are optional services that will be performed if Bioverativ selects collaboration compounds for lead optimization. The amount paid by Bioverativ for the services during the Joint Research Team do not reflect a discount that the customer would otherwise receive and do not provide the customer with material rights.

The total transaction price was determined to be $14.2 million, consisting of the $10.0 million upfront payment and non-refundable research and development funding of $4.2 million. The Company may receive reimbursement of FTE costs and external costs associated with work under the Joint Research Term, milestone payments during the Joint Research Term, as well as upon exercise of the license options. These variable amounts are excluded from the transaction price as they relate to fees and milestones that can only be achieved subsequent to the exercise of an option.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the Research License and Related Services is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin what would be expected to be realized under similar contracts. The estimated standalone selling price for the material rights was determined based on the fees Bioverativ would pay to exercise the license options, the estimated value of the license option using comparable transactions, and the probability that the license options would be exercised by

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

Bioverativ. Based on the relative standalone selling price, the allocation of the transaction price to the separate performance obligations is as follows (in thousands):

Performance Obligations	Allocation of Transaction Price
Sickle Cell Research License and Related Services	$ 1,405
Hemophilia Research License and Related Services	2,811
Sickle Cell License Option Material Right	5,286
Hemophilia License Option Material Right	4,698
	$ 14,200

The Company will recognize revenue related to amounts allocated to the Sickle Cell and Hemophilia Research License and Related Services obligations as the underlying services are performed using a proportional performance model, over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent time expected, which best reflects the progress towards satisfaction of the performance obligation. The amount allocated to the material rights is recorded as deferred revenue and the Company will commence revenue recognition when the underlying option is exercised or upon expiry of the option.

For the years ended December 31, 2017 and 2018, the Company recognized $0.4 million and $4.0 million, respectively, of collaboration revenue related to its collaboration with Bioverativ. As of December 31, 2017 and 2018, the Company recorded deferred revenue of $14.5 million and $9.9 million, respectively, related to its collaboration with Bioverativ, respectively.

Oxurion Collaboration Agreement

Summary of Agreement

In August 2013, the Company entered into a Research Collaboration and License Agreement (the "Oxurion Collaboration Agreement") with Oxurion . Under the Oxurion Collaboration Agreement, the Company is responsible for identifying Bicycle peptides related to the collaboration target, plasma kallikrein, for use in various ophthalmic indications. Oxurion is responsible for further development and product commercialization after the defined research screening is performed by the Company.

Under the Oxurion Collaboration Agreement, the Company is obligated to perform specified research activities in accordance with the research plan, which includes two stages. Stage I, now completed, focused on the screening of targets using the Company's Bicycle peptide discovery platform with the goal of identifying compounds that meet the criteria set by the parties, and Stage II, now underway, during which Oxurion has continued research activities on selected Bicycle peptides with the goal of identifying compounds for further development and commercialization. The Company is not obligated or expected to perform any research services during Stage II of the research plan.

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

The Company granted certain worldwide intellectual property rights to Oxurion for the development, manufacture and commercialization of licensed compounds associated with plasma kallikrein. The Oxurion Collaboration Agreement provided for an upfront payment of €1.0 million and potential additional R&D funding, at an agreed upon FTE rate, should the research effort require more than one FTE or the research plan be amended or extended by Oxurion. In addition, Oxurion is required to make certain milestone payments to the Company upon the achievement of specified research, development, regulatory and commercial events. More specifically, for each collaboration program, the Company is eligible to receive up to €8.3 million in research and development milestones of which €1.8 million has been received as of December 31, 2018. In addition, the Company is eligible to receive up to €16.5 million upon achievement of certain regulatory milestone payments (e.g. €5 million for granting first regulatory approval in either the United States or EU for the first indication). In addition, to the extent any of the collaboration products covered by the licenses granted to Oxurion are commercialized, the Company would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from Oxurion.

Either party may terminate the Oxurion Collaboration Agreement if the other party has materially breached any of its material obligations and such breach continues after the specified cure period. Either party may terminate the Oxurion Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. Oxurion may terminate the Oxurion Collaboration Agreement, entirely or on a program by program, licensed product by licensed product or country by country basis, for convenience upon not less than 90 days prior written notice to the Company.

In November 2017, the parties executed the First Deed of Amendment to the Oxurion Collaboration Agreement ("First Amendment"). The First Amendment confirms that THR-149 has been selected as a development compound under the Oxurion Collaboration Agreement and that Stage II of the research plan has been completed. The First Amendment provided for additional research services to be performed by the Company related to the identification of two additional compounds for Oxurion, in its discretion, to select as development compounds. As for the work under the Oxurion Collaboration Agreement, the Company will perform the work under Stage I of the research plan which will be funded at a specified FTE rate, plus any direct out of pocket expenses, and Oxurion will be responsible for Stage II research and any development after the selection of a development compound. Additional milestones and royalties were added for the potential additional licensed compounds, consistent with those of the initial Oxurion Collaboration Agreement. The Company is not obligated or expected to perform any research services during Stage II of the research plan.

Accounting Analysis

Under the Oxurion Collaboration Agreement, all licenses were granted and research services to be provided by the Company were fully completed and revenue associated with those obligations was fully recognized prior to January 1, 2016. Under the First Amendment, the Company has identified a single performance obligation associated with the performance of

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Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

research services associated with Stage I of the research plan for which the Company will be reimbursed for its services at a specified FTE reimbursement rate plus out of pocket costs which will be recognized on a proportional performance basis as the associated FTE efforts and costs are incurred, which best reflects the progress towards satisfaction of the performance obligation. None of the unpaid development or regulatory milestones have been included in the transaction price, as all milestone are not considered probable at December 31, 2017 and December 31, 2018.

For the years ended December 31, 2017 and 2018, the Company recognized $0.8 million and $1.7 million, respectively, of revenue related to its agreements with Oxurion. As of December 31, 2018, the research services under the First Amendment were complete. The revenue recognized for the twelve months ended December 31, 2017 and 2018 includes $0.8 million and $1.2 million, respectively, related to the achievement of developmental milestones during the advancement of the research by Oxurion into a Phase I clinical study. There was no deferred revenue recorded as of December 31, 2017 and 2018 in connection with the agreements with Oxurion.

Summary of Contract Assets and Liabilities

Up-front payments and fees are recorded as deferred revenue upon receipt or when due until such time as the Company satisfies its performance obligations under these arrangements. A contract asset is a conditional right to consideration in exchange for goods or services that the Company has transferred to a customer. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

The following table presents changes in the balances of the Company's contract assets and liabilities (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Impact of Exchange Rates	Balance at End of Period
Period ended December 31, 2017					
Contract assets	$ —	$ —	$ —	$ —	$ —
Contract liabilities:					
Deferred revenue					
Bioverativ collaboration deferred revenue	—	14,200	(355)	622	14,467
Total deferred revenue	$ —	$ 14,200	$ (355)	$ 622	$ 14,467

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

	Balance at Beginning of Period	Additions	Deductions	Impact of Exchange Rates	Balance at End of Period
Period ended December 31, 2018					
Contract assets	$ —	$ 91	$ (91)	$ —	$ —
Contract liabilities:					
Deferred revenue					
Bioverativ collaboration deferred revenue	14,467	—	(4,006)	(553)	9,908
AstraZeneca collaboration deferred revenue		5,350	(466)	(157)	4,727
Total deferred revenue	$ 14,467	$ 5,350	$ (4,472)	$ (710)	$ 14,635

The contract assets represents research and development services which have been performed but have not yet been billed, and are reduced when they are subsequently billed.

The Bioverativ deferred revenue balance at December 31, 2018 is comprised of $9.9 million allocated to the Sickle Cell License Option Material Right and Hemophilia License Option Material Right, which will commence revenue recognition when the respective option is exercised at the end of Joint Research Term or when the option expires.

The AstraZeneca deferred revenue balance includes $4.7 million allocated to the Target 3, Target 4, Target 5 and Target 6 Material Rights, which will commence revenue recognition when the respective option is exercised at the end of AZ Research Term or when the option expires. The remaining balance relates to research and development services billed in advance that will be recognized over the Bicycle Research Term.

During the year ended December 31, 2017 and 2018, the Company recognized the following revenues as a result of changes in the contract asset and the contract liability balances in the respective periods (in thousands):

	Year Ended December 31,	
	2017	2018
Revenue recognized in the period from:		
Revenue recognized based on proportional performance	$ (355)	$ (4,472)

Cancer Research UK

On December 13, 2016, the Company entered into a Clinical Trial and License Agreement with Cancer Research Technology Limited ("CRTL") and Cancer Research UK ("CRUK"). Pursuant to the agreement, as amended in March 2017 and June 2018, CRUK's Centre for Drug Development will sponsor and fund a Phase Ia and Phase IIa clinical trial for the Company's lead product candidate, BT1718, a Bicycle Toxin Conjugate, in patients with advanced solid tumors.

CRUK is responsible to design, prepare, carry out and sponsor the clinical trial at its cost. The Company is responsible for supplying agreed quantities of GMP materials for the study, the supply

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

of which has been completed. In the event that additional quantities are needed, the Company will provide CRUK with all reasonable assistance to complete the arrangements necessary for the generation and supply of such additional GMP materials but CRUK will be responsible for supplying and paying for such additional quantities of GMP materials.

The Company granted CRUK a license to its and its affiliates' intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial the Company retains the right to continue the development of BT1718 during the clinical trial. Upon the completion of the Phase I/IIa clinical study, the Company has the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and the Company decides to abandon development of all products that deliver cytotoxic payloads to the MT1 target antigen, the Company will assign or grant to CRTL an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case the Company will receive a mid to high double digit percentage of the net revenue depending on the stage of development when the license is granted). The CRUK agreement contains additional future milestone payments upon the achievement of development and regulatory milestones, payable in cash and shares, with an aggregate total value of $50.9 million, as well as royalty payments based on a high double digit percentage on net sales of products developed.

The CRUK agreement can be terminated by either party upon an insolvency event, material breach of the terms of the contract, or upon a change in control (and the new controlling entity generates its revenue from the sale of tobacco products or is an affiliate of such party). CRUK may terminate the arrangement for safety reasons or if it determines that the objectives of the clinical trial will not be met, in which case, if the study is terminated by CRUK prior to the completion of the Phase 1a dose escalation portion of the study for such reasons or if CRUK refuses release of any additional quantities of GMP materials or if the parties cannot agree upon a plan to supply the additional quantities of GMP materials, the Company will be obligated to refund fifty percent of the costs and expenses incurred or committed by CRUK to perform the clinical trial. If the study is terminated by CRUK for an insolvency event, a material breach by the Company, or if the Company is acquired by an entity that generates its revenue from the sale of tobacco products or is an affiliate of such party, the Company will reimburse CRUK in full for all costs paid or committed in connection with the clinical trial and no further license payments, where applicable, shall be due. In such case where we are acquired by an entity that generates its revenue from the sale of tobacco products or is an affiliate of such party, CRUK will not be obliged to grant a license to the Company in respect of the results of the clinical trial and the Company will assign or grant to CRT an exclusive license to develop and commercialize the product without CRT being required to make any payment to the Company.

The Company concluded that the costs incurred by CRUK is a liability in accordance with ASC 730, Research and Development, as the payment is not based solely on the results of the research and development having future economic benefit. As such, the Company recorded a liability of $0.3 million and $0.8 million at December 31, 2017 and 2018, respectively, which is recorded in other long-term liabilities in the consolidated balance sheets. The liability is recorded as incremental research and development expense in the statements of operations and comprehensive loss.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

11. Income Taxes

The components of net loss before tax provision from income taxes are as follows (in thousands):

	Year Ended December 31,	
	2017	2018
	(as restated)	
United Kingdom	$ (16,319)	$ (22,229)
United States	37	(13)
Total	$ (16,282)	$ (22,242)

The components of the benefit for income taxes are as follows (in thousands):

	Year Ended December 31,	
	2017	2018
	(as restated)	
Current income tax provision (benefit)		
Federal	$ 75	$ (25)
State	10	7
Total current income tax provision (benefit)	85	(18)
Deferred income tax (benefit) provision		
Federal	(58)	(167)
State	(50)	(211)
Total deferred income tax (benefit)	(108)	(378)
Total benefit from income taxes	$ (23)	$ (396)

A reconciliation of the provision (benefit) for income taxes computed at the statutory income tax rate to the provision (benefit) for income taxes as reflected in the financial statement is as follows:

	Year Ended December 31,	
	2017	2018
	(as restated)	
Benefit for income taxes at statutory rate	19%	19%
(Decreases) increases resulting from:		
Federal tax credits	0.4%	1.1%
Change in valuation allowance	(9.4)%	(7.2)%
Net losses surrendered for research credit	(6.7)%	(3.7)%
Preferred share warrants	(1.1)%	(0.6)%
Other	(2.1)%	(6.8)%
Effective income tax rate	0.1%	1.8%

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

11. Income Taxes (Continued)

Significant components of the Company's current and deferred tax assets at December 31, 2017 and 2018, were as follows (in thousands):

	Year Ended December 31,	
	2017 (as restated)	2018
Deferred tax assets:		
Operating loss carryforwards	$ 4,209	$ 4,953
Research credit carryforwards	—	197
Accrued expenses and other	247	1,149
Total deferred tax assets	4,456	6,299
Deferred tax liabilities:		
Depreciation & amortization	(143)	(163)
Total deferred tax liabilities	(143)	(163)
Valuation allowance	(4,175)	(5,621)
Net deferred tax assets	$ 138	$ 515

During the years ended December 31, 2017 and 2018, the Company recorded an income tax benefit of $23,000 and $0.4 million, respectively. The Company is subject to United Kingdom corporate taxation. Due to the nature of its business, the Company has generated losses since inception and has therefore not paid United Kingdom corporation tax. The Company's income tax benefit is mainly the result of deferred tax assets benefitted in the United States that do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement.

On December 22, 2017, the Tax Cuts and Jobs Act (the "TCJA") was signed into United States law. The TCJA included a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from a top marginal tax rate of 35% to a flat rate of 21%, effective as of January 1, 2018, as well as limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). The federal tax rate change resulted in a reduction in the amount of the Company's deferred tax assets and liabilities recorded as of December 31, 2017 of $21,000. As a result, $21,000 of tax expense was recognized as of the enactment date of the TCJA.

On December 22, 2017, the Securities and Exchange Commission issued guidance under Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act directing taxpayers to consider the impact of the U.S. legislation as "provisional" when it does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete its accounting for the change in tax law.

In connection with the initial analysis of the impact of the TCJA, the Company remeasured its deferred tax assets and liabilities based on the rates at which they are expected to reverse in the

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

11. Income Taxes (Continued)

future, which is generally 21% for federal tax purposes. During the year ended December 31, 2018, the Company did not make any adjustments to the provisional amounts recorded as a result of the TCJA of $21,000 recorded in the year ended December 31, 2017 and the Company considers the accounting related to the TCJA to be final.

The Company regularly assesses its ability to realize its deferred tax assets. Assessing the realization of deferred tax assets requires significant judgment. In determining whether its deferred tax assets are more likely than not realizable, the Company evaluated all available positive and negative evidence, and weighed the evidence based on its objectivity. After consideration of the evidence, including the Company's history of cumulative net losses in the U.K., and has concluded that it is more likely than not that the Company will not realize the benefits of its U.K. deferred tax assets and accordingly the Company has provided a valuation allowance for the full amount of the net deferred tax assets in the U.K. The Company has considered the Company's history of cumulative net profits in the United states, estimated future taxable income and concluded that it is more likely than not that the Company will realize the benefits of its United State deferred tax assets and has not provided a valuation allowance against the net deferred tax assets in the United States. The valuation allowance increased for the year ended December 31, 2017 by $1.8 million due to the corresponding increase in UK deferred tax assets, primarily due to operating loss carryforwards generated during the year. The valuation allowance increased in the year ended December 31, 2018 by $1.4 million due to the corresponding increase in UK deferred tax assets, primarily due to operating loss carryforwards generated during the year that were not surrendered for research credit utilization.

The Company recorded a valuation allowance against all of its U.K. deferred tax assets as of December 31, 2017 and 2018.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2017 and 2018 related primarily to the increase in net operating loss carryforwards and research and development tax credit carryforwards in 2017 and 2018 and were as follows (in thousands):

	Year Ended December 31,	
	2017 (as restated)	2018
Valuation allowance as of beginning of year	$ 2,402	$ 4,175
Increases recorded to income tax provision	1,773	1,446
Valuation allowance as of end of year	$ 4,175	$ 5,621

The Company intends to continue to maintain a full valuation allowance on its U.K. deferred tax assets until there is sufficient evidence to support the reversal of all or some portion of these allowances. The release of the valuation allowance would result in the recognition of certain deferred tax assets and an increase to the benefit for income taxes for the period the release is recorded. However, the exact timing and amount of the valuation allowance release are subject to change on the basis of the level of profitability that the Company is able to actually achieve.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

11. Income Taxes (Continued)

The benefit for income taxes shown on the consolidated statements of operations differs from amounts that would result from applying the statutory tax rates to income before taxes primarily because of certain permanent expenses that were not deductible, U.K., federal and state research and development credits, as well as the application of valuation allowances against the U.K. deferred tax assets.

As of December 31, 2017, the Company had $24.8 million of U.K. operating loss carryforwards and $0 of federal and state net operating loss carryforwards. As of December 31, 2018, the Company had $29.1 million of U.K. operating loss carryforwards and $0 of U.S. federal and state net operating loss carryforwards. The U.K. operating loss carryforwards have an indefinite life. As of December 31, 2018, the Company had $60,000 and $0.1 million of federal and state research and development credit carryforwards, respectively, that expire at various dates through 2038.

The Company recognizes, in its consolidated financial statements, the effect of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained upon examination. The Company had no uncertain tax positions during the years ended of December 31, 2017 and 2018. There are no amounts of interest or penalties recognized in the consolidated statement of operations or accrued on the consolidated balance sheet for any period presented. The Company does not expect any material changes in these uncertain tax benefits within the next 12 months.

The Company files income tax returns in the United Kingdom, and in the United States for federal income taxes and in the Commonwealth of Massachusetts for state income taxes. In the normal course of business, the Company is subject to examination by tax authorities in these jurisdictions. The 2017 tax year remains open to examination the by HM Revenue & Customs. The statute of limitations for assessment with the Internal Revenue Service is generally three years from filing the tax return. As such, all years since inception in the U.S. remain open to examination. The Company is currently not under examination by jurisdictions for any tax years.

12. Commitments and Contingencies

In September 2015, the Company entered into a tenancy agreement for space in Building 260 Babraham Research Campus, Cambridge, UK for a period of two years, beginning on October 1, 2015. The annual rent was approximately $0.2 million plus service charges. In October 2017 this agreement was extended until January 2018 with annual rent of approximately $0.2 million.

In January 2017, Bicycle Therapeutics Inc. entered into a lease for office and laboratory space in Cambridge, Massachusetts for the period from February 1, 2017 to December 31, 2017. Rental payments under the lease were $19,500 per month, plus a portion of the landlords operating costs.

In September 2017, Bicycle Therapeutics Inc. entered into a lease agreement for office and laboratory space in Lexington, Massachusetts, which commenced on January 1, 2018 and expires on December 31, 2022. The rent expense, inclusive of the escalating rent payments, is recognized on a straight-line basis over the lease term. Bicycle Therapeutics Inc. has the option to extend the lease agreement for a successive period at a market based rental rate. In conjunction with the lease agreement, Bicycle Therapeutics Inc. paid a security deposit $0.2 million as well as prepaid rent of

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

$0.1 million for the first month of the third, fourth and fifth year of the lease. The deposit and prepaid rent balances are recorded in other assets in the consolidated balance sheets.

In October 2017, the Company entered into a lease agreement for office and laboratory space in Building 900, Babraham Research Campus, Cambridge, UK, which expires on December 21, 2021. The annual rent is approximately $0.5 million. The Company has the right to renew the lease for five years commencing December 21, 2021 which would be subject to a day one rent review. Service charges are also payable based on floor area and are estimated to be approximately $0.1 million per year. In conjunction with the lease agreement, the Company paid a security deposit $0.6 million, which is recorded in other assets in the consolidated balance sheets.

The Company recorded rent expense of $0.5 million and $1.0 million, during the years ended December 31, 2017 and 2018, respectively.

The following table summarizes the future minimum lease payments due under the Company's operating leases as of December 31, 2018 (in thousands):

2019	888
2020	901
2021	915
2022	483
2023	—
	$ 3,187

The Company has entered into various agreements with contract manufacturing organizations to provide clinical trial materials and with vendors for preclinical research studies, synthetic chemistry and other services for operating purposes. These payments are not included in the table of contractual obligations above since the contracts are generally cancelable at any time upon less than 90 days' prior written notice. The Company is not contractually able to terminate for convenience and avoid any and all future obligations to these vendors. Under such agreements, the Company is contractually obligated to make certain minimum payments to the vendors, with the payments in the event of a termination with less than 90 days' notice based on the timing of the termination and the exact terms of the agreement.

Legal proceedings

From time to time, the Company or its subsidiaries may become involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business.

In September 2016, the Company filed a complaint in the District Court of the Hague against Pepscan Systems B.V. ("Pepscan") to contest the right of Pepscan to terminate a non-exclusive patent license agreement we entered into with Pepscan in 2009 and 2010 ("PLA"). In response, Pepscan counterclaimed for injunctive relief and unquantified damages. The Company is vigorously prosecuting its claims and defending against those of Pepscan. The Company does not believe that a loss is probable or estimable at this time, and as such, the Company has not recorded a liability related to the Pepscan litigation as of December 31, 2017 or at December 31, 2018. Should the

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

Company not be successful in maintaining its rights to Pepscan's patent or in the Company's alternative demand that the patent be invalidated, commercialization of the Company's lead product could be delayed. As the Pepscan patent expires prior to the expected commercialization date of the product, the Company does not believe that the legal proceedings could have a material adverse effect on the Company's business and operating results.

Founder Royalty arrangements

At the time BicycleRD Limited was organized, BicycleRD Limited entered into a royalty agreement with its founders and initial investors (the "Founder Royalty Agreement"). Pursuant to the Founder Royalty Agreement, the Company will pay a royalty rate in the low single digit percentages on net product sales to its founders and initial investors, for a period of 10 years from the first commercial sale on a country by country basis. No royalties have been earned or paid under the royalty arrangements to date.

In accordance with the terms of the Founder Royalty Agreements, as amended in May 2017, the parties amended the terms of the royalty arrangements to limit the future royalties payments to net sales on future products that could be generated under the collaboration with Oxurion and AstraZeneca, in exchange for the issuance of warrants to subscribe for 200,000 Series A Preferred Shares. The Company recorded the fair value of the warrants to subscribe for Series A Preferred Shares to the founders of $0.9 million as research and development expense during the year ended December 31, 2017, as the licenses do not have alternative future use, in accordance with ASC Topic 730, *Research and Development*.

Indemnification obligations

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has indemnification obligations towards members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification arrangements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnification obligations. The Company is not aware of any claims under indemnification arrangements, and therefore it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2017 and 2018.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

13. Net loss and unaudited pro forma net loss per share

Net loss per share

Basic and diluted net loss per share attributable to ordinary shareholders was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2017	2018
	(as restated)	
Numerator:		
Net loss attributable to ordinary shareholders	$ (16,259)	$ (21,846)
Denominator:		
Weighted average ordinary shares outstanding, basic and diluted	333,125	438,862
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (48.81)	$ (49.78)

The Company's potentially dilutive securities, which include share options, convertible preferred shares and warrants to subscribe for Series A and Series B1 Preferred Shares, and unvested restricted shares, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of ordinary shares outstanding used to calculate both basic and diluted net loss per share attributable to ordinary shareholders is the same. The Company excluded the following potentially dilutive ordinary shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to ordinary shareholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2017	2018
Convertible preferred shares (as converted to ordinary shares)	9,641,740	11,532,659
Warrants to subscribe for convertible preferred shares (as adjusted to reflect the impact of the share capital reorganization and issuance of bonus shares (Note 1))	1,347,953	1,347,953
Restricted ordinary shares	162,466	83,947
Options to purchase ordinary shares	964,538	863,712
	12,116,697	13,828,271

Unaudited pro forma net loss per share attributable to ordinary shareholders

The unaudited pro forma basic and diluted net loss per share attributable to ordinary shareholders for the year ended December 31, 2018 (unaudited) have been prepared to give effect to adjustments arising upon the completion of the proposed IPO as if the IPO had occurred on January 1, 2018. The unaudited pro forma net loss attributable to ordinary shareholders used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to ordinary

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

13. Net loss and unaudited pro forma net loss per share (Continued)

shareholders does not include the effects the change in fair value of the warrant liability because the calculation gives effect to (i) the conversion of all outstanding convertible preferred shares into ordinary shares upon the completion of an IPO and (ii) the exercise of 200,000 warrants to subscribe for Series A convertible preferred shares immediately prior to an IPO, and (iii) the exercise of the warrants to subscribe for 371,645 Series B1 convertible preferred shares (Note 7), as if the proposed IPO had occurred on the later of January 1, 2018 or the issuance date of the convertible preferred shares and the warrants to subscribe for convertible preferred shares.

	Year Ended December 31, 2018 (unaudited)
Numerator:	
Net loss attributable to ordinary shareholders	$ (21,846)
Change in fair value of preferred stock warrant liability	665
Pro forma net loss attributable to ordinary shareholders	$ (21,181)
Denominator:	
Weighted average ordinary shares outstanding, basic and diluted	438,862
Pro forma adjustment to reflect the weighted average conversion of all outstanding convertible preferred shares into ordinary shares upon the completion of an IPO as adjusted to reflect the impact of the share recapitalization and issuance of bonus shares (Note 1)	9,698,571
Pro forma adjustment to reflect the exercise of warrants to subscribe for convertible preferred shares which expire upon the completion of an IPO	816,877
Pro forma weighted average ordinary shares outstanding, basic and diluted	10,954,310
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted	$ (1.93)

14. Benefit plans

The Company established a defined-contribution savings plan under Section 401(k) of the Code (the "401(k) Plan"). The 401(k) Plan covers all U.S. employees and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the 401(k) Plan may be made at the discretion of the Company's board of directors. During the years ended December 31, 2017 and 2018 the Company made contributions totaling $42,000 and $0.1 million, respectively, to the 401(k) Plan.

The Company provides a pension contribution plan for its employees in the United Kingdom, pursuant to which the Company may match employees contributions each year ("U.K Plan"). During the years ended December 31, 2017 and 2018 the Company made contributions totaling $0.2 million and $0.2 million, respectively, to the U.K. Plan.

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

15. Related party transactions

The Company has entered into Founder Royalty Agreements with its founders and initial investors (Note 12). No royalties have been earned or paid under the Founder Royalty Agreements to date.

The Chairman of the Company's Board of Directors is associated with 10X Capital Inc., who provided consultancy services to the Company totaling $0.1 million and $0.2 million during the years ended December 31, 2017 and 2018, respectively.

16. Geographic information

The Company operates in two geographic regions: the United States and the United Kingdom. Information about the Company's long-lived assets held in different geographic regions is presented in the table below (in thousands):

	December 31,	
	2017	2018
United States	$ 395	$ 498
United Kingdom	967	1,320
	$ 1,362	$ 1,818

The Company's collaboration revenues are attributed to the operations of the Company in the United Kingdom.

17. Subsequent events

For the consolidated financial statements as of and for the year ended December 31, 2018, the Company evaluated subsequent events through March 22, 2019, the date on which those financial statements were issued.

On January 3, 2019, the Company completed the issue of 80,385 Series B2 preferred shares at a price per Series B2 preferred share of £15.55, for gross cash proceeds of $1.6 million.

On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will expire.

On May 9, 2019, the Company's board of directors and shareholders approved the following corporate actions:

- the reorganization of the Company's share capital, effective on May 13, 2019, by issuing ordinary shares as bonus shares to each holder of ordinary shares on the basis of 1.429 bonus shares for each ordinary share in issue (having the effect of a one for 1.429 share split without having an impact on the nominal value of the ordinary shares);

- upon the closing of a firm commitment underwritten public offering in which the aggregate proceeds raised in the offering equal or exceed $50 million, the Company's Series A and Series B1 Preferred Shares and Series B2 Preferred Shares will be automatically converted

Bicycle Therapeutics Limited

Notes to Consolidated Financial Statements (Continued)

17. Subsequent events (Continued)

into ordinary shares at the applicable conversion price adjusted accordingly for the share split;

Events assessed for disclosure subsequent to the original issuance of the consolidated financial statements (unaudited).

In March 2019, Bioverativ exercised its right to terminate the Sickle cell program. The Company will recognize the portion of the transaction price allocated to the Sickle Cell License Option Material Right (Note 10) as revenue in the first quarter of 2019, as its performance obligation is complete.

On May 9, 2019, the Company's board of directors and shareholders approved the following corporate actions:

- the authorized number of ordinary shares was increased from 15,452,420 to 31,995,653;
- the adoption of the 2019 Share Option and Incentive plan, or the 2019 Plan, which will become effective immediately prior to the effectiveness of the registration statement on Form S-1 related to the Company's initial public offering. The 2019 Plan provides for the grant of options to purchase ordinary shares, share appreciation rights, restricted shares, restricted share units, and other share-based awards, and 2,470,583 additional ordinary shares are reserved under the 2019 Plan;
- the adoption of the 2019 Employee Share Purchase Plan, which will become effective upon the closing of the Company's initial public offering. An additional 215,000 ordinary shares will become available for future issuance under this plan;
- the authorization for management to re-register the Company as a public company limited by shares with the name Bicycle Therapeutics Plc.

Bicycle Therapeutics Limited

Consolidated Balance Sheets

(amounts in thousands, except share and per share data)

(unaudited)

	December 31, 2018	March 31, 2019	Pro Forma March 31, 2019
Assets			
Current assets:			
Cash	$ 63,380	$ 59,364	$ 59,371
Accounts receivable	5,021	260	260
Prepaid expenses and other current assets	2,076	2,224	2,224
Research and development incentives receivable	6,292	8,071	8,071
Total current assets	76,769	69,919	69,926
Property and equipment, net	1,818	1,801	1,801
Operating lease right-of-use assets	—	2,588	2,588
Other assets	3,039	3,486	3,486
Total assets	$ 81,626	$ 77,794	$ 77,801
Liabilities, convertible preferred shares and shareholders' (deficit) equity			
Current liabilities:			
Accounts payable	$ 1,887	$ 2,241	$ 2,241
Accrued expenses and other current liabilities	7,032	6,154	6,154
Deferred revenue, current portion	10	24	24
Total current liabilities	8,929	8,419	8,419
Warrant liability	4,804	8,101	—
Deferred revenue, net of current portion	14,625	9,580	9,580
Operating lease liabilities	—	1,837	1,837
Other long-term liabilities	897	1,050	1,050
Total liabilities	29,255	28,987	20,886
Commitments and contingencies (Note 12)			
Series A convertible preferred shares, £0.01 nominal value; 3,000,001 shares authorized at December 31, 2018 and March 31, 2019; 2,800,001 shares issued and outstanding at December 31, 2018 and March 31, 2019; liquidation value of $35,753 and $36,484 at December 31, 2018 and March 31, 2019, respectively; no shares authorized, issued or outstanding, pro forma as of March 31, 2019	41,820	41,820	—
Series B1 convertible preferred shares, £0.01 nominal value; 4,690,485 shares authorized at December 31, 2018 and March 31, 2019; 3,947,198 shares issued and outstanding at December 31, 2018 and March 31, 2019; liquidation value of $57,460 and $58,635 at December 31, 2018 and March 31, 2019, respectively; no shares authorized, issued or outstanding, pro forma as of March 31, 2019	54,621	54,621	—
Series B2 convertible preferred shares, £0.01 nominal value; 1,403,633 shares authorized at December 31, 2018 and March 31, 2019; 1,323,248 and 1,403,633 shares issued and outstanding at December 31, 2018 and March 31, 2019, respectively; liquidation value of $26,274 and $28,440 at December 31, 2018 and March 31, 2019, respectively; no shares authorized, issued or outstanding, pro forma as of March 31, 2019	25,756	27,339	—
Shareholders' (deficit) equity:			
Ordinary shares, £0.01 nominal value; 15,452,450 shares authorized at December 31, 2018 and March 31, 2019; 898,675 and 898,678 shares issued at December 31, 2018 and March 31, 2019, respectively; 814,728 and 842,035 shares outstanding at December 31, 2018 and March 31, 2019, respectively; 13,363,084 shares issued and 13,306,441 shares outstanding, pro forma at March 31, 2019	10	11	173
Additional paid-in capital	1,857	2,132	133,858
Accumulated other comprehensive loss	(1,751)	(671)	(671)
Accumulated deficit	(69,942)	(76,445)	(76,445)
Total shareholders' (deficit) equity	(69,826)	(74,973)	56,915
Total liabilities, convertible preferred shares and shareholders' (deficit) equity	$ 81,626	$ 77,794	$ 77,801

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

(unaudited)

	Three Months Ended March 31,	
	2018	2019
Collaboration revenues	$ 2,808	$ 6,384
Operating expenses:		
Research and development	3,709	6,276
General and administrative	1,988	3,402
Total operating expenses	5,697	9,678
Loss from operations	(2,889)	(3,294)
Other income (expense):		
Interest and other income (expense)	(3)	64
Other expense, net	(38)	(3,193)
Total other expense, net	(41)	(3,129)
Net loss before income tax provision	(2,930)	(6,423)
Provision for (benefit from) income taxes	(396)	80
Net loss	$ (2,534)	$ (6,503)
Net loss attributable to ordinary shareholders	$ (2,534)	$ (6,503)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (6.38)	$ (7.80)
Weighted average ordinary shares outstanding, basic and diluted	397,483	834,043
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted		$ (0.25)
Pro forma weighted average number of ordinary shares outstanding, basic and diluted		13,293,400
Comprehensives Loss:		
Net loss	$ (2,534)	$ (6,503)
Other comprehensive income (loss):		
Foreign currency translation adjustment	1,796	1,080
Total comprehensive loss	$ (738)	$ (5,423)

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited
Consolidated Statements of Convertible Preferred Shares and Shareholders' (Deficit) Equity
(In thousands, except share amounts)
(Unaudited)

	Series A Convertible Preferred Shares		Series B1 Convertible Preferred Shares		Series B2 Convertible Preferred Shares		Ordinary Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2017	2,800,001	$ 41,820	3,947,198	$ 54,621	—	—	368,995	$ 5	$ 838	$ 69	$ (48,096)	$ (47,184
Issuance of restricted share awards	—	—	—	—	—	—	35,725	1	53	—	—	54
Issuance of ordinary shares upon exercise of share options	—	—	—	—	—	—	9,002	—	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	198	—	—	198
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	1,796	—	1,796
Net loss	—	—	—	—	—	—	—	—	—	—	(2,534)	(2,534
Balance at March 31, 2018	2,800,001	$ 41,820	3,947,198	$ 54,621	—	—	413,722	$ 6	$ 1,089	$ 1,865	$ (50,630)	$ (47,670
Balance at December 31, 2018	2,800,001	$ 41,820	3,947,198	$ 54,621	1,323,248	$ 25,756	814,728	$ 10	$ 1,857	$ (1,751)	$ (69,942)	$ (69,826
Issuance of convertible preferred shares	—	—	—	—	80,385	1,583	—	—	—	—	—	—
Issuance of restricted share awards	—	—	—	—	—	—	27,304	1	103	—	—	104
Issuance of ordinary shares upon exercise of share options	—	—	—	—	—	—	3	—	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	172	—	—	172
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	1,080	—	1,080
Net loss	—	—	—	—	—	—	—	—	—	—	(6,503)	(6,503
Balance at March 31, 2019	2,800,001	$ 41,820	3,947,198	$ 54,621	1,403,633	$ 27,339	842,035	$ 11	$ 2,132	$ (671)	$ (76,445)	$ (74,973
Conversion of convertible preferred shares to ordinary shares	(2,800,001)	(41,820)	(3,947,198)	(54,621)	(1,403,633)	(27,339)	11,647,529	151	123,629	—	—	123,780
Conversion of warrant liability to equity	—	—	—	—	—	—	816,877	11	8,097	—	—	8,108
Pro forma balance at March 31, 2019	—	$ —	—	$ —	—	$ —	13,306,441	$ 173	$ 133,858	$ (671)	$ (76,445)	$ 56,915

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited

Consolidated Statements of Cash Flows

(In thousands)

(unaudited)

	Three Months Ended March 31,	
	2018	**2019**
Cash flows from operating activities:		
Net loss	$ (2,534)	$ (6,503)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	252	276
Depreciation and amortization	166	213
Change in fair value of warrant liability	38	3,197
Changes in operating assets and liabilities:		
Accounts receivable	(1,671)	4,860
Research and development incentives receivable	(835)	(1,650)
Prepaid expenses and other current assets	(397)	(215)
Operating lease right-of-use assets	—	176
Other assets	(380)	125
Accounts payable	(394)	415
Accrued expenses and other current liabilities	(539)	(783)
Lease liabilities	—	(176)
Deferred revenue	(1,118)	(5,327)
Other long-term liabilities	139	191
Net cash used in operating activities	(7,273)	(5,201)
Cash used in investing activities:		
Purchases of property and equipment	(264)	(418)
Net cash used in investing activities	(264)	(418)
Cash flows from financing activities:		
Proceeds from issuance of series B2 convertible preferred shares, net of issuance costs	—	1,334
Payments of initial public offering costs	—	(1,300)
Net cash provided by financing activities	—	34
Effect of exchange rate changes on cash	2,432	1,569
Net decrease in cash	(5,105)	(4,016)
Cash at beginning of period	67,663	63,380
Cash at end of period	$ 62,558	$ 59,364
Supplemental disclosure of cash flow information		
Deferred initial public offering costs accrued but not paid	—	431
Cash paid for amounts included in the measurement of operating lease liabilities	—	224

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements

1. Basis of presentation

Basis of presentation

The accompanying consolidated financial statements include the accounts of Bicycle Therapeutics Limited and its wholly owned subsidiaries, BicycleTx Limited, BicycleRD Limited and Bicycle Therapeutics Inc. All intercompany balances and transactions have been eliminated on consolidation.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP").

The accompanying consolidated balance sheet as of March 31, 2019, consolidated statements of operations and comprehensive loss, statements of cash flows, and the consolidated statements of convertible preferred shares and shareholders' (deficit) equity for the three months ended March 31, 2018 and 2019 are unaudited. The unaudited interim consolidated financial statements have been prepared on the same basis as the audited annual consolidated financial statements as of and for the year ended December 31, 2018, and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of March 31, 2019, and the results of its operations and its cash flows for the three months ended March 31, 2018 and 2019. The financial data and other information disclosed in these notes related to the three months ended March 31, 2018 and 2019 are also unaudited.

The results for the three months ended March 31, 2019 are not necessarily indicative of results to be expected for the year ending December 31, 2019, any other interim periods, or any future year or periods. These interim financial statements should be read in conjunction with the audited financial statements as of and for the year ended December 31, 2018, and the notes thereto, which are included elsewhere in this Registration Statement.

In May 2019, the Company's board of directors and shareholders approved the reorganization of the Company's share capital by issuing ordinary shares as bonus shares to each holder of ordinary shares on the basis of 1.429 bonus shares for each ordinary share in issue (having the effect of a one for 1.429 share split (without having an impact on the nominal value of the ordinary shares)), which was effected on May 13, 2019. All issued and outstanding share and per share amounts of ordinary shares and share options included in the accompanying consolidated financial statements have been adjusted to reflect this share split for all periods presented. In addition, the number of ordinary shares that will be issued to the holders of the Company's convertible preferred shares (Note 6) and warrants to subscribe for Series A and Series B1 convertible preferred shares (Note 7) in conjunction with the closing of the IPO has been adjusted accordingly, as well as the number of ordinary shares over which options have been granted.

Liquidity

The accompanying consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Through December 31, 2018 and March 31, 2019, the Company has funded its operations primarily with proceeds from sales of convertible preferred shares (Note 6) and proceeds received from its collaboration arrangements (Note 10). Since inception, the Company has incurred recurring losses, including net losses of $21.8 million for the year ended

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

1. Basis of presentation (Continued)

December 31, 2018 and $6.5 million for the three months ended March 31, 2019. As of December 31, 2018 and March 31, 2019, the Company had an accumulated deficit of $69.9 million and $76.4 million, respectively. The Company expects to continue to generate operating losses in the foreseeable future.

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements — Going Concern,* the Company has evaluated whether there are certain conditions and events, considered in the aggregate, that raise substantial doubt and the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. As of May 13, 2019, the issuance date of the the interim consolidated financial statements for the three months ended March 31, 2019, the Company expects that its cash will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the issuance date of the interim consolidated financial statements.

The Company is seeking to complete an initial public offering ("IPO") of its ordinary shares in the form of American Depositary Shares. Upon the completion of a public offering with at least £50.0 million of gross proceeds and at a price of at least £31.10 per share, subject to appropriate adjustment in the event of any share split or other similar recapitalization (a "Qualified IPO"), the Company's outstanding convertible preferred shares will automatically convert into ordinary shares (Note 6).

In the event the Company does not complete an IPO, the Company expects to seek additional funding through private equity financings, collaborations, government grants, strategic alliances and or licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborations. The terms of any future financing may adversely affect the rights or interests of the Company's shareholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects.

Although management continues to pursue these plans, there can be no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

2. Summary of Significant Accounting Policies

The Company's significant accounting policies are disclosed in the audited consolidated financial statements for the year ended December 31, 2018 included in the Company's audited financial statements included within its Form S-1. Since the date of such consolidated financial statements, there have been no changes to the Company's significant accounting policies, other than those disclosed below.

Unaudited pro forma information

On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will be extinguished (Note 7). The accompanying unaudited pro forma consolidated

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

balance sheet and consolidated statements of convertible preferred shares and shareholders' (deficit) equity as of March 31, 2019 has been prepared to give effect, upon the closing of a Qualified IPO, to (i) the automatic conversion of all outstanding convertible preferred shares as of March 31, 2019 into ordinary shares, and (ii) the exercise of 200,000 warrants to subscribe for Series A convertible preferred shares immediately prior to an IPO, and (iii) the exercise of the 371,645 warrants to subscribe for Series B1 convertible preferred shares, as well as (iv) the resulting reclassification of the warrant liability to additional paid-in capital, as if the proposed IPO had occurred on March 31, 2019.

In the accompanying consolidated statements of operations and comprehensive loss, the unaudited pro forma basic and diluted net loss per share attributable to ordinary shareholders for the three months ended March 31, 2019 have been prepared to give effect, upon the closing of a Qualified IPO, to (i) the automatic conversion of all outstanding shares of convertible preferred shares into ordinary shares, and (ii) the exercise of 200,000 warrants to subscribe for Series A convertible preferred shares immediately prior to an IPO, and (iii) the exercise of the warrants to subscribe for 371,645 Series B1 convertible preferred shares which would otherwise expire upon the completion of an IPO, as if the proposed IPO had occurred on the later of January 1, 2019 or the issuance date of the convertible preferred shares or preferred share warrants.

Leases

The Company determines if an arrangement is a lease at inception. Operating leases are included in operating lease right-of-use ("ROU") assets, other current liabilities, and operating lease liabilities in the Company's consolidated balance sheet. The Company has not entered into any financing leases.

ROU assets represent the Company's right to use and control an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. The ROU asset also includes lease payments made before the lease commencement date and excludes any lease incentives. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option.

The components of a lease shall be split into three categories, if applicable: lease components (e.g., land, building, etc.), non-lease components (e.g., common area maintenance, maintenance, consumables, etc.), and non-components (e.g., property taxes, insurance, etc.). The fixed and in-substance fixed contract consideration (including any related to non-components) must then be allocated based on fair values to the lease components and non-lease components. The Company's facilities operating leases may have lease and non-lease components to which the Company has elected to apply a practical expedient to account for each lease component and related non-lease component as one single component. The lease component results in a right-of-use asset being recorded on the balance sheet. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Government grants

From time to time, the Company may enter into arrangements with governmental entities for the purposes of obtaining funding for research and development activities. The Company recognizes government grant funding in the consolidated statements of operations and comprehensive loss as the related expenses being funded are incurred. The Company classifies government grants received under these arrangements as a reduction to the related research and development expense incurred. The Company analyzes each arrangement on a case-by-case basis. For the three months ended March 31, 2019, the Company recognized $0.1 million, as a reduction of research and development expense related to government grant arrangements. There were no grant proceeds recognized for the three month period ended March 31, 2018.

Recently adopted accounting pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"). This guidance revises existing practice related to accounting for leases under ASC Topic 840 Leases ("ASC 840"). ASU 2016-02 requires lessees to recognize most leases on their balance sheet as a right-of-use asset and a lease liability. The lease liability is equal to the present value of lease payments and the right-of-use asset is based on the lease liability, subject to adjustment such as for initial direct costs. For income statement purposes, the new standard retains a dual model similar to ASC 840, requiring leases to be classified as either operating or finance. For lessees, operating leases will result in straight-line expense (similar to current accounting by lessees for operating leases under ASC 840). In July 2018, the FASB issued ASU No. 2018-11, *Leases (Topic 842) Targeted Improvements*, which provides an additional transition method that allows entities to initially apply the new standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption without restating prior periods. The guidance is effective for annual reporting periods beginning after December 15, 2018 and interim periods within those fiscal years, and early adoption is permitted. The Company adopted the new standard on January 1, 2019 by applying the new lease requirements at the adoption date without restating prior periods. In connection with the adoption of ASU 2016-02 the Company recorded an impact of approximately $2.7 million on its unaudited consolidated balance sheet to record right-of-use-assets and $2.6 million to record lease liabilities on January 1, 2019, which are primarily related to the lease of the Company's corporate headquarters in the U.K. and the lease of its office and laboratory space in Lexington, MA. The adoption of ASU 2016-02 did not have a material impact on the Company's results of operations or cash flows.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation — Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07") to simplify the accounting for share-based payments to non-employees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The new guidance expands the scope of ASC 718, *Compensation — Stock Compensation*, to include share-based payments granted to non-employees in exchange for goods or services used or consumed in an entity's own operations and supersedes the guidance in ASC Topic 505-50, *Equity-Based Payments to Non-Employees*. The guidance is effective for public business entities in annual periods beginning after December 15, 2018 and interim periods within those years. Early adoption is permitted. The Company adopted the new standard on January 1, 2019. The adoption did not have a material impact on the Company's financial position, results of operations or cash flows.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

3. Fair value of financial assets and liabilities

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis (in thousands):

	Fair Value Measurement as of December 31, 2018 using:			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Warrant liability	$ —	$ —	$ 4,804	$ 4,804
	$ —	$ —	$ 4,804	$ 4,804

	Fair Value Measurement as of March 31, 2019 using:			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Warrant liability	$ —	$ —	$ 8,101	$ 8,101
	$ —	$ —	$ 8,101	$ 8,101

The warrant liability was initially recorded at fair value upon the date of the warrants' issuance and is subsequently remeasured to fair value at each reporting date (Note 7).

During the year ended December 31, 2018 and the three months ended March 31, 2019, there were no transfers between levels.

4. Property and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31, 2018	March 31, 2019
Laboratory equipment	$ 3,356	$ 3,562
Leasehold improvements	75	77
Computer equipment	221	227
Furniture and office equipment	99	119
	3,751	3,985
Less: Accumulated depreciation and amortization	(1,933)	(2,184)
	$ 1,818	$ 1,801

Depreciation expense was $0.2 million and $0.2 million for the three months ended March 31, 2018 and 2019, respectively.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

5. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2018	March 31, 2019
Accrued employee compensation and benefits	$ 1,610	$ 607
Accrued external research and development expenses	3,814	3,885
Income taxes payable	15	8
Accrued professional fees	1,494	1,058
Current portion of operating lease liabilities	—	584
Other	99	12
	$ 7,032	$ 6,154

6. Convertible preferred shares

The Company has issued Series A convertible preferred shares ("Series A Preferred Shares"), Series B1 convertible preferred shares ("Series B1 Preferred Shares"), and Series B2 convertible preferred shares ("Series B2 Preferred Shares") (collectively the "Preferred Shares").

On May 26, 2017 the Company completed the issue of 3,562,583 Series B1 Preferred Shares at a price per share of £11.2278, for gross cash proceeds of $51.9 million. In addition, on October 27, 2017, an additional unaffiliated investor subscribed for a further 384,615 Series B1 Preferred Shares at a price per share of £13, for gross cash proceeds of $6.6 million. These two transactions are collectively referred to as "the Series B1 Financing". In conjunction with the Series B1 Financing, the Company also issued warrants to subscribe for 743,287 Series B1 Preferred Shares to the subscribers of the Series B1 Preferred Shares (Note 7). The Company allocated a portion of the proceeds equal to the fair value of the warrants at the date of grant to the warrant liability, and the remaining amount was allocated to the Series B1 Preferred Shares.

On December 20, 2018, the Company completed the issue of 1,323,248 Series B2 preferred shares at a price per Series B2 preferred share of £15.55, for gross cash proceeds of $26.1 million (the "Series B2 Financing"). In conjunction with the Series B2 Financing, the existing holders of warrants to subscribe for Series B1 preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 preferred shares and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 preferred shares to the new investor. In conjunction with the Series B2 Financing, the Company designated all previously outstanding Series B preferred shares as Series B1 preferred shares. On January 3, 2019, the Company completed the issue of 80,385 Series B2 preferred shares at a price per share of £15.55, for gross cash proceeds of $1.6 million.

The rights, preferences, and privileges of the Preferred Shares are described below:

Voting rights

The holders of Preferred Shares are entitled to vote, together with the holders of ordinary shares, on all matters submitted to shareholders for a vote, except as required by law. Each preferred shareholder is entitled to the number of votes equal to the number of ordinary shares into which each preferred share is convertible as of the date of the vote.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

6. Convertible preferred shares (Continued)

Liquidation preferences

In the event that the Company liquidates, dissolves or winds up, whether voluntarily or involuntarily, the Company sells all or substantially all of its assets or businesses, or the Company sells the whole or any part of the issued share capital of a subsidiary, the shareholders of the Company sell a controlling interest in the Company, or if certain events deemed to be a liquidation occur, then the holders of the Series B2 Preferred Shares are entitled to receive in preference to the holders of the Series B1 Preferred Shares, the Series A Preferred Shares and the ordinary shares an amount per share equal to the original purchase price of the Series B2 Preferred Shares, plus any dividends, if declared but unpaid thereon. In addition, following payment of the preference to the holders of Series B2 Preferred Shares, the holders of the Series B1 Preferred Shares are entitled to receive in preference to the holders of the Series A Preferred Shares and the ordinary shares an amount per share equal to the original purchase price of each respective Series B1 Preferred Share, plus any dividends, if declared but unpaid thereon. In addition, following payment of the preference to the holders of Series B1 Preferred Shares, the holders of the Series A Preferred Shares are entitled to receive in preference to the holders of the ordinary shares, an amount per share equal to the original purchase price of each respective Series A Preferred Share, plus any dividends, if declared but unpaid thereon. Following all preferential payments to holders of the Preferred Shares, as required, any remaining undistributed assets are shared ratably with the holders of the ordinary shares and the convertible preferred shares with the latter's share number being determined on an "as-if-converted" basis.

Dividends

The holders of the Preferred Shares rank pari passu in all respects as to dividends with the holders of the ordinary shares. The Company may not pay any dividends on ordinary shares of the Company unless the holders of Preferred Shares then outstanding simultaneously receive dividends at the same rate and same time as dividends paid with respect to ordinary shares. Through December 31, 2018 and March 31, 2019, no dividends have been declared or paid.

Redemption rights

The Preferred Shares are not redeemable at the option of the holder.

The holders of Preferred Shares have liquidation rights in the event of a deemed liquidation that, in certain situations such as a change in control, are not solely within the control of the Company. Therefore, convertible preferred shares are classified outside of shareholders' (deficit) equity.

Conversion rights

Each Preferred Share is convertible at any time at the option of the shareholder into fully paid ordinary shares. Each Preferred Share will be automatically converted into such number of ordinary shares, at the applicable conversion ratio then in effect, upon either (i) the closing of a firm commitment public offering with at least £50.0 million of gross proceeds and at a price of at least £31.10 per share, subject to appropriate adjustment in the event of any share split, share dividend, combination or other similar recapitalization, or (ii) the vote or written consent of the holders of at least a 77% of the outstanding Preferred Shares on an as converted basis, voting together as a single class.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

6. Convertible preferred shares (Continued)

The Preferred Shares are initially convertible to ordinary shares on a one for one basis, subject to adjustment for certain dilutive events and certain capital reorganizations in accordance with the terms of the articles of association of the Company.

Upon issuance of each class of Preferred Shares, the Company assessed the embedded conversion and liquidation features of the securities. The Company determined that each class of Preferred Shares does not require the Company to separately account for the conversion or liquidation features. The Company also concluded that no beneficial conversion features existed upon the issuance date of the Series A Preferred Shares, Series B1 Preferred Shares, or Series B2 Preferred Shares.

7. Warrant liability

On May 26, 2017, the Company issued 200,000 warrants to subscribe for Series A Preferred Shares at £0.01 each which are exercisable at any time after May 26, 2017 provided that they have not otherwise lapsed in accordance with their terms. The warrants were issued as consideration to amend a royalty arrangement (Note 12) with certain founders of the Company. The Company recorded the fair value of the warrants to subscribe for Series A Preferred Shares to the founders of $0.9 million as research and development expense at the time of issuance in May 2017, as the underlying license rights do not have alternative future use, in accordance with ASC Topic 730, Research and Development.

The warrants to subscribe for Series A Preferred Shares expire upon the earlier of (i) 10 years from their issuance date, or (ii) upon an IPO or exit unless an exercise delay notice is provided by the Series A warrant holder, in which case they will expire 12 months following an IPO or exit.

On May 26, 2017, in conjunction with the issuance of 3,562,583 Series B1 Preferred Shares at a price per share of £11.2278 (Note 6), the Company issued 627,903 warrants to subscribe for Series B1 Preferred Shares with an exercise price of £0.01. In addition, on October 27, 2017, in conjunction with the issuance of 384,615 Series B1 Preferred Shares the Company issued a further 115,384 warrants to subscribe for Series B1 Preferred Shares with an exercise price of £0.01. In conjunction with the Series B2 Financing (Note 6), the existing holders of warrants to subscribe for Series B1 preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 preferred shares and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 preferred shares to the new investor.

The warrants to subscribe for Series B1 Preferred Shares may be exercised from the first to occur of (i) March 31, 2020, (ii) upon notification of an equity fund raise for aggregate proceeds of a minimum amount to be determined by the board of directors of the Company, (iii) the notification of initiation of an IPO, (iv) notification of an exit (being either: (a) a sale or other transfer of the whole or any part of the issued share capital of the Company or any subsidiary on an arm's length basis that results in such person (along with any persons acting in concert) holding a controlling interest in the Company or any subsidiary; or (b) the disposition of all or substantially all of the assets or business of the Company to a third party (either by way of a sale, license and/or other transfer), or (v) upon an unfavorable outcome related to a patent complaint (Note 12). The Series B1 Warrants expire upon five years from becoming exercisable, or immediately prior to an exit (having the meaning set out above in this paragraph), IPO, an equity fund raise (having the meaning set out above in this paragraph), upon a favorable judgment related to a patent complaint

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

7. Warrant liability (Continued)

(Note 12), or upon the winding up of the Company. The warrants to purchase Series B1 preferred shares contain limitations on their ability to be exercised based on the status of the patent complaint, in accordance with the terms of the warrant agreement.

The warrants to subscribe for Series A and Series B1 Preferred Shares are recorded as a liability and remeasured to fair value at each reporting date (Note 3). Changes in the fair value of the warrant liability are recognized as other expense, net in the consolidated statements of operations and comprehensive loss. The following table provides a roll-forward of the fair values of the Company's warrant liability for which fair value is determined by Level 3 inputs (in thousands):

	Warrant Liability
Fair value at December 31, 2018	$ 4,804
Change in fair value of warrant liability recorded as other expense	3,197
Impact of exchange rates on translation of warrant liability to USD included in accumulated other comprehensive income (loss)	100
Fair value at March 31, 2019	$ 8,101

In conjunction with the Series B2 Financing (Note 6), in December 2018, the existing holders of warrants to subscribe for Series B1 preferred shares surrendered 194,911 warrants to subscribe for the same number of Series B1 preferred shares and the Company issued a further 194,911 warrants to subscribe for the same number of Series B1 preferred shares to the new investor. The transfer of warrants between investors did not have an impact to the valuation of the warrant liability, as this represents a transaction between shareholders and the Company did not issue any new instruments or change the rights and preferences of the underlying warrants to subscribe for Series B1 preferred shares.

On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will expire. The Company assessed this event as a modification to the terms of the Series B1 warrants and, remeasured the warrant liability immediately before and immediately after the modification, which resulted in an incremental change in fair value of $0.1 million, which is included in other expenses for the three months ended March 31, 2019.

The warrant liability in the table above consisted of the fair value of warrants to subscribe for Series A and Series B1 Preferred Shares (see Note 6) and was based on significant inputs not observable in the market, which represent a Level 3 measurement within the fair value hierarchy. The Company's valuation of the warrants to subscribe for Series A and Series B1 Preferred Shares utilized the Black-Scholes option-pricing model, which incorporates assumptions and estimates to value the warrant liability. The Company assesses these assumptions and estimates on a quarterly basis as additional information impacting the assumptions is obtained.

The quantitative elements associated with the Company's Level 3 inputs impacting the fair value measurement of the warrant liability include the fair value per share of the underlying Series A and Series B1 preferred shares into which the warrant is exercisable, the remaining contractual term

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

7. Warrant liability (Continued)

of the warrants, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying convertible preferred shares.

The most significant assumption in the Black-Scholes option-pricing model impacting the fair value of the warrant liability is the fair value of the Series A and Series B1 preferred shares into which the warrant is exercisable as of each remeasurement date. Given the absence of an active market for the Company's equity securities, Company determines the fair value per share of the convertible preferred shares underlying the warrants by taking into consideration the implied value derived from an independent third-party valuation of the Company's ordinary shares, adjusted for certain restrictions on the exercise of the B1 warrants per their contractual terms. Assumptions related to the remaining term, free interest rate, expected dividend yield and expected volatility do not have an impact to the fair value of the warrants because the exercise price of the warrants is £0.01, and the fair value of the warrant is equal to the difference between the exercise price and the fair value regardless of the assumptions. The Company historically has been a private company and lacks company-specific historical and implied volatility information of its shares. Therefore, it estimates its expected share volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrants. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrants. The Company has estimated a 0% dividend yield based on the expected dividend yield and the fact that the Company has never paid or declared dividends. The following table presents the unobservable inputs to the fair value measurement of the warrant liability:

	December 31, 2018		March 31, 2019	
	Series A Warrants	Series B1 Warrants[1]	Series A Warrants	Series B1 Warrants[2]
Risk free rate	2.6%	2.5%	2.5%	2.5%
Expected dividend yield	—%	—%	—%	—%
Expected term (years)	8.4	6.25	8.2	6.0
Expected volatility	75.4%	79.6%	74.4%	78.0%
Exercise price	£ 0.01	£ 0.01	£ 0.01	£ 0.01
Fair value preferred share underlying the warrant	$ 8.61	$ 4.15	$ 14.23	$ 12.91

(1) The fair value of the Series B1 preferred shares underlying the warrants to purchase Series B1 preferred shares at December 31, 2018 includes a 50% probability that the warrants will be not be exercisable prior to the IPO, based on their contractual terms.

(2) On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will expire.

8. Ordinary shares

Each holder of ordinary shares is entitled to one vote per ordinary share and to receive dividends when and if such dividends are recommended by the board of directors and declared by the shareholders. As of December 31, 2018 and March 31, 2019, the Company has not declared any dividends.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

8. Ordinary shares (Continued)

As of December 31, 2018 and March 31, 2019, the Company's authorized capital share capital consisted of 15,452,420 ordinary shares with a nominal value of £0.01 per share.

9. Share-based compensation

Employee incentive pool

The Company is authorized to issue ordinary shares, as well as options and other securities exercisable for or convertible into ordinary shares, as incentives to its employees, consultants, and members of its board of directors. To the extent such incentives are in the form of share options, the options may have been granted pursuant to a potentially tax-favored Enterprise Management Incentive, or EMI, scheme available to U.K. employees, directors and consultants of the Company. The issuance of share options and ordinary shares is administered by the board of directors using standardized share option and share subscription agreements.

As of December 31, 2018 and March 31, 2019, the Company was authorized to issue a total of 2,302,442 ordinary shares under a reserve set aside for equity awards. As of December 31, 2018 and March 31, 2019, there were 694,534, and 627,382 ordinary shares available for future issuance to the Company's employees, consultants and members of the board of directors, respectively. Awards of restricted ordinary shares, which are referred to as employee shares, are subject to vesting. Unvested employee shares are subject to repurchase upon termination of employment.

Options granted, as well as restricted shares granted as employee incentives, typically vest over a four-year service period with 25% of the award vesting on the first anniversary of the commencement date and the balance thereafter in 36 equal monthly instalments, and expire no later than 10 years from the date of grant.

Certain equity awards were issued in 2017 for which 20% of the award vests upon the first anniversary of the vesting start date, 60% vests thereafter in 36 equal monthly installments, and 20% vest upon the earlier of the fourth anniversary of the vesting start date, or the achievement of a specified revenue threshold from the Company's collaboration arrangements. Options granted generally expire 10 years from the date of grant.

Options issued to U.K. employees have an exercise price of £0.01 per share. The exercise price for share options granted to U.S. employees, which are not subject to the EMI schemes, have an exercise price that is not less than the fair value of ordinary shares as determined by the board of directors as of the date of grant. The Company's board of directors values the Company's ordinary shares based on input from management, considering the most recently available valuation of ordinary share performed by an independent third-party valuation firm as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

9. Share-based compensation (Continued)

Share-based compensation

The Company recorded share-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss (in thousands):

	Three Months Ended March 31,	
	2018	**2019**
Research and development expenses	$ 128	$ 108
General and administrative expenses	124	168
	$ 252	$ 276

Share options

The following table summarizes the Company's option activity since December 31, 2018:

	Number of Shares	**Weighted Average Exercise Price**	**Weighted Average Contractual Term**	**Aggregate Intrinsic Value**
			(in years)	**(in thousands)**
Outstanding as of December 31, 2018	863,712	$ 1.01	8.75	$ 3,292
Granted	122,316	3.54		
Exercised	(3)	0.01		
Forfeited	(55,164)	1.57		
Outstanding as of March 31, 2019	930,861	$ 1.33	8.68	$ 6,492
Vested and expected to vest as of March 31, 2019	930,861	$ 1.33	8.68	$ 6,492
Options exercisable as of March 31, 2019	244,200	$ 1.41	8.20	$ 1,685

The weighted average grant-date fair value of share options granted during the three months ended March 31, 2018 and 2019 was $1.94 per share and $3.68 per share, respectively.

For the three months ended March 31, 2018 and 2019, the Company recorded share-based compensation expense for share options granted of $0.2 million and $0.2 million, respectively. Expense for non-employee consultants for the three months ended March 31, 2018 and 2019, was immaterial.

The aggregate intrinsic value of share options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares. The

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

9. Share-based compensation (Continued)

aggregate intrinsic value of share options exercised during the three months ended March 31, 2018 and 2019 was $24,000 and $0 respectively.

During the three months ended March 31, 2018 and 2019, the Company granted options for the purchase of an aggregate of 18,719 and 0 ordinary shares, respectively, for which 20% of the award vests upon the first anniversary of the vesting start date, 60% vests thereafter in 36 equal monthly installments, and 20% on the earlier of the fourth anniversary of the vesting start date, or the achievement of a specified revenue threshold from the Company's collaboration arrangements. The Company concluded that the accelerated vesting condition was not probable at March 31, 2018. The Company recorded expense of $0.2 million and $0.1 million, during the three months ended March 31, 2018 and 2019, respectively, related to these awards.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the fair value of share options granted to employees and directors:

	Three Months Ended March 31,	
	2018	2019
Risk-free interest rate	1.3%	2.7%
Expected volatility	75.1%	79.6%
Expected dividend yield	—	—
Expected term (in years)	6.07	6.07

As of March 31, 2019, total unrecognized compensation expense related to the unvested employee and director share-based awards was $1.6 million, which is expected to be recognized over a weighted average period of 3.2 years.

Restricted shares

The Company has granted restricted shares with service-based vesting conditions. Shares of unvested restricted shares may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award. These restricted shares are subject to repurchase rights, for aggregate consideration of £1. Accordingly, the Company has recorded the proceeds from the issuance of restricted shares as a liability in the consolidated balance sheets included as a component of accrued expenses and other current liabilities. The restricted share liability is reclassified into shareholders' (deficit) equity as the restricted shares vest.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

9. Share-based compensation (Continued)

The following table summarizes the Company's restricted ordinary share award activity since December 31, 2018:

	Shares	Weighted Average Grant-Date Fair Value
Unvested restricted ordinary shares as of December 31, 2018	83,947	$ 1.93
Issued	—	—
Forfeited	—	—
Vested	(27,304)	1.71
Unvested restricted ordinary shares as of March 31, 2019	56,643	$ 2.10

For the three months ended March 31, 2018 and 2019, the Company recorded share-based compensation expense of $0.1 million and $0.1 million, respectively, for unvested restricted shares granted.

The fair value of employee restricted share awards vested during the three months ended March 31, 2018 and 2019, based on estimated fair values of the ordinary shares underlying the restricted share awards on the day of vesting, was $0.1 million and $0.1 million, respectively.

As of March 31, 2019, total unrecognized compensation cost related to the unvested employee and director restricted share awards was $0.1 million, which is expected to be recognized over a weighted average period of 1.8 years.

10. Significant Agreements

For the three months ended March 31, 2018 and 2019, the Company had collaboration agreements with AstraZeneca, Bioverativ, and Oxurion. The following table summarizes the revenue recognized in the Company's consolidated statements of operations and comprehensive loss from these arrangements (in thousands):

	Three Months Ended March 31,	
	2018	2019
Collaboration revenues		
AstraZeneca	$ 300	$ 425
Bioverativ	1,118	5,959
Oxurion	1,390	—
Total collaboration revenues	$ 2,808	$ 6,384

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

AstraZeneca Collaboration Agreement

Summary of Agreement — 2016 Agreement

In November 2016, the Company entered into a Research Collaboration Agreement (the "AstraZeneca Collaboration Agreement") with AstraZeneca. The collaboration is focused on the research and development of Bicycle peptides that bind to up to six biological targets. After discovery and initial optimization of such Bicycle peptides, AstraZeneca will be responsible for all research and development, including lead optimization and drug candidate selection. AstraZeneca has option rights, at drug candidate selection, which allow it to obtain development and exploitation license rights with regard to such drug candidate. The initial research obligation focuses on two targets within respiratory, cardiovascular and metabolic disease. AstraZeneca also has an option to nominate up to four additional targets at any point up to the second anniversary of the agreement ("Additional Four Target Option"). The exercise of this option right results in an option fee payable to the Company of $5.0 million and the research obligations and rights are consistent with the obligations and rights related to the initial two targets discussed below.

Under the AstraZeneca Collaboration Agreement, the Company is obligated to use commercially reasonable efforts to perform research activities on the initial two targets, under mutually agreed upon research plans. The research plans includes two discrete parts, on a research program by research program basis: (i) the Bicycle Research Term, which is focused on the generation of Bicycle peptide libraries using the Company's peptide drug discovery platform, to be screened against selected biological targets and optimization of promising compounds, with the goal of identifying compounds that meet the criteria set by the parties, and (ii) the AZ Research Term, during which AstraZeneca may select certain compounds and continue research activities on those compounds, at its sole expense, with the goal of identifying compounds that satisfy the relevant pharmacological and pharmaceutical criteria for clinical testing. AstraZeneca may, at its sole discretion, approve any compound to be progressed into drug development and, upon the selection of each drug candidate, AstraZeneca is to pay $8.0 million as an option fee, in order to obtain worldwide development and exploitation rights.

Each research program is to continue for an initial period of three years (the "Research Term"), including one year for the Bicycle Research Term and two for the AZ Research Term. AstraZeneca may extend the Research Term for each research program by twelve months (or fifteen months, if needed to complete certain toxicology studies). The Research Term for a specific program can be shorter if it is ceased due to a screening failure, a futility determination, abandonment by AstraZeneca, or upon selection of a drug candidate. AstraZeneca has certain substitution rights should a screening failure or futility determination be reached but is obligated to fund these additional efforts related to substitution.

Under the terms of the AstraZeneca Collaboration Agreement, the Company granted to AstraZeneca, for each research program, a right and license (with the right to sublicense) certain background and platform intellectual property, for the duration of the applicable Research Term, to the extent necessary or useful for AstraZeneca to conduct the activities assigned to it in the applicable research plan, but for no other purpose.

The activities under the AstraZeneca Collaboration Agreement are governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

AstraZeneca. The JSC oversees and reviews each research program. Among other responsibilities, the JSC monitors and reports on research progress and ensure open and frequent exchange between the parties regarding research program activities.

AstraZeneca is obligated to fund two full time equivalents ("FTE") during the Bicycle Research Term, for each research program, based on an agreed upon FTE reimbursement rate. Payment is made quarterly in advance of services being provided.

AstraZeneca has the option to obtain development and commercialization licenses associated with each designated drug candidate in return for a fee of $8.0 million per drug candidate. In addition, AstraZeneca is required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial milestones. More specifically, for each research program, the Company is eligible to receive up to $29.0 million in development milestone payments and up to $23.0 million in regulatory milestone payments. The Company is also eligible for up to $110.0 million in commercial milestone payments, on a research program by research program basis. Development milestone payments are triggered upon initiation of a defined phase of clinical research for a drug candidate. Regulatory milestone payments are triggered upon approval to market a product candidate by the United States Food and Drug Administration ("FDA") or other global regulatory authorities. Commercial milestone payments are triggered when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. In addition, to the extent any of the product candidates covered by the licenses conveyed to AstraZeneca are commercialized, the Company would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including in certain countries where AstraZeneca faces generic competition. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from AstraZeneca.

Either party may terminate the AstraZeneca Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. Either party may terminate the AstraZeneca Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. AstraZeneca may terminate the AstraZeneca Collaboration Agreement, entirely or on a licensed product by licensed product or country by country basis, for convenience.

Accounting Analysis

The Company has identified the following performance obligations:

(i) research license and the related research and development services during the Bicycle Research Term for the first target (the "Target One Research License and Related Services"),

(ii) research license and the related research and development services during the Bicycle Research Term for the second target (the "Target Two Research License and Related Services").

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

The Company concluded that the Additional Four Target Option is not a material right, as the option does not provide a discount that AstraZeneca otherwise would not have received. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract. The Company has concluded that the research license is not distinct from the research and development services during the Bicycle Research Term as AstraZeneca cannot obtain the benefit of the research license without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as it relates to constrained peptide technology that is not available in the marketplace. As a result, for each research program, the research license has been combined with the research and development services into a single performance obligation.

The total transaction price was initially determined to be $1.2 million, consisting solely of research and development funding. The Company utilizes the most likely amount method to determine the amount of research and development funding to be received. Additional consideration to be paid to the Company upon the exercise of the license options by AstraZeneca or upon reaching certain milestones is excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the option exercise or are outside of the initial contact term.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the Target One and Target Two Research License and Related Services is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin what would be expected to be realized under similar contracts. The transaction price allocated to each performance obligation was initially $0.6 million.

The Company will recognize revenue related to amounts allocated to the Research License and Related Services as the underlying services are performed over the one year Research Term using a proportional performance model over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent time expected and will remeasure its progress towards completion at the end of each reporting period, which best reflects the progress towards satisfaction of the performance obligation.

In October 2017, AstraZeneca selected a replacement target for the first target, and as such a new Research Term was started related to the Target One Research License and Related Services. In addition, both programs were extended. The total transaction price under the arrangement increased to $2.0 million for the additional research and development funding to be received.

For the three months ended March 31, 2018 and 2019, the Company recognized $0.3 million and $0.2 million, respectively, of collaboration revenue related to the Target One and Target Two Research License and Related Services for its Collaboration Agreement with AstraZeneca. As of December 31, 2018 and March 31, 2019, the Company recorded $8,000 and $24,000 of deferred revenue, respectively, in connection with the 2016 AstraZeneca Collaboration Agreement.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

May 2018 AstraZeneca Option Exercise — Additional Four Targets

Under the AstraZeneca Collaboration Agreement, AstraZeneca was granted an option to nominate up to four additional targets at any point up to the second anniversary of the agreement ("Additional Four Target Option"). In May 2018, AstraZeneca made an irrevocable election to exercise the Additional Four Target Option. As a result, AstraZeneca is entitled to obtain research and development services with respect to Bicycle peptides that bind to up to four additional targets, along with license rights to those selected targets, in exchange for an option fee of $5.0 million to be paid by AstraZeneca to the Company no later than January 31, 2019. AstraZeneca is obligated to fund two FTEs during the Bicycle Research Term, for each research program, based on an agreed upon FTE reimbursement rate. Payment is made quarterly in advance of services being provided. AstraZeneca has the option to obtain worldwide development and commercialization licenses associated with each designated drug candidate in return for a fee of $8.0 million per drug candidate, upon the selection of such drug candidate, after which AstraZeneca would be required to fund development and commercialization costs, and to pay regulatory and commercial milestone payments and royalties to BicycleTX as for the other products developed under the AstraZeneca Collaboration Agreement.

Accounting Analysis

Upon the execution of the agreement, the Company has identified the following five performance obligations associated with the AstraZeneca May 2018 Agreement:

(i) Research license and the related research and development services during the Bicycle Research Term for the third target (the "Target Three Research License and Related Services"),

(ii) Material right associated with the development and exploitation license option for the third target ("Target Three Material Right"),

(iii) Material right associated with the research services option, including the underlying development and exploitation license option for the fourth target ("Target Four Material Right"),

(iv) Material right associated with the research services option, including the underlying development and exploitation license option for the fifth target ("Target Five Material Right"), and

(v) Material right associated with the research services option, including the underlying development and exploitation license option for the sixth target ("Target Six Material Right").

The Company concluded that the fourth, fifth and sixth targets available for selection are options. Upon exercise, AstraZeneca will obtain a research license and the related research and development services and an option to a development and exploitation license. The Company has concluded that the research services option, including the underlying development and exploitation license options related to each respective target results in a material right as the option exercise fee related to the development and exploitation license contains a discount that AstraZeneca would not have otherwise received.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

The research license and the related research and development services related to the fourth, fifth and sixth targets are not performance obligations, as they are optional services that will be performed if AstraZeneca selects additional targets and they reflect their standalone selling prices and do not provide the customer with material rights. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract.

The total transaction price was determined to be $5.7 million, consisting of the $5.0 million option exercise fee and research and development funding of an estimated $0.7 million. The research and development funding is being provided based on the costs that are incurred to conduct the research and development services. The Company utilizes the most likely amount method to determine the amount of research and development funding to be received. Additional consideration to be paid to the Company upon the exercise of the license options by AstraZeneca or upon reaching certain milestones are excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the license option exercise or are outside of the initial contact term.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for each Research License and Related Services obligation is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin what would be expected to be realized under similar contracts. The estimated standalone selling price for the material rights was determined based on the fees AstraZeneca would pay to exercise the license options, the estimated value of the License Option using comparable transactions, and the probability that (i) AstraZeneca would opt into the target development, and (ii) the license options would be exercised by AstraZeneca. Based on the relative standalone selling price, the allocation of the transaction price to the separate performance obligations at the inception of the arrangement is as follows (in thousands):

Performance Obligations	Allocation of Transaction Price
Target Three Research License and Related Services	$ 650
Target 3 Material Right	1,504
Target 4 Material Right	1,204
Target 5 Material Right	1,165
Target 6 Material Right	1,127
	$ 5,650

The Company will recognize revenue related to amounts allocated to the Target Three Research License and Related Services as the underlying services are performed using a proportional performance model over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent time expected, which best reflects the progress towards satisfaction of the performance obligation. The amount allocated to the material rights is recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the option. The optional future research license and the related research and development services related to the fourth, fifth and sixth targets reflect their standalone selling prices and do not provide the customer with a material right

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Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

and, therefore, are not considered performance obligations and are accounted for as separate contracts. During the three months ended March 31, 2019, the Company commenced research and development services related to the fourth target.

For the three months ended March 31, 2019, the Company recognized $0.3 million of revenue related to the Target Three Research License and Related Service related to the May 2018 AstraZeneca Option Exercise and research and development services related to the fourth target. As of December 31, 2018 and March 31, 2019, the Company recorded $4.7 million and $4.8 million of deferred revenue in connection with the May 2018 AstraZeneca Option Exercise and related contracts, respectively.

Bioverativ Collaboration Agreement

Summary of Agreement

In August 2017, the Company entered into a Collaboration Agreement (the "Bioverativ Collaboration Agreement") with Bioverativ. Under the Bioverativ Collaboration Agreement the Company will provide for research and development services focused on up to three collaboration programs; (i) Sickle cell disease, (ii) Hemophilia, and (iii) and a third program ("Program 3"), which is an optional program, to be defined. The Company will use its bicyclic peptide screening platform to perform research and development services for the programs and Bioverativ has the ability to select a collaboration product for each program and obtain a license to develop and exploit the selected collaboration product for an additional option fee.

Under the Bioverativ Collaboration Agreement, the Company is obligated to perform research activities on the initial two named collaboration programs, under mutually agreed upon research plans. The research and development services for each program consist of two stages. The first is an initial stage of screening for high affinity binders and affinity maturation of such binders to identify lead compounds led by the Company (the "BV Bicycle Research Term"). Upon the conclusion of the BV Bicycle Research Term, Bioverativ can, at is sole discretion, select a certain number of collaboration compounds to move forward into the Joint Research Term. Upon selection of the collaboration compounds, Bioverativ is required to pay an option fee. During the Joint Research Term, the Company and Bioverativ will jointly conduct research and development activities which will include lead optimization of lead compounds, in preparation for lead collaboration product nomination ("Joint Research Term"). Bioverativ may, at its sole discretion, approve any compound to be progressed into drug development and upon the selection of each collaboration product candidate, Bioverativ shall pay $5.0 million as an option fee, in order to obtain worldwide development and exploitation rights for that collaboration product.

Each research program shall continue for an initial period of three years (the "Research Term") unless a program is abandoned by Bioverativ or extended for up to one year. The first year of each Research Term shall be the BV Bicycle Research Term and the remaining part of the Research Term, including any extensions of the Research Term, shall be the Joint Research Term.

Under the terms of the Bioverativ Collaboration Agreement, the Company granted to Bioverativ, for each collaboration program, a non-exclusive, sublicensable (through multiple tiers), worldwide license under certain intellectual property of the Company to conduct the activities

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

assigned to Bioverativ in the applicable research plan for the duration of the applicable Research Term, but for no other purpose.

The activities under the Bioverativ Collaboration Agreement will be governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and Bioverativ. The JSC will oversee, review and recommend direction of each collaboration program and variations of or modifications to the research plans.

Under the terms of the Bioverativ Collaboration Agreement, the Company received a $10.0 million up-front cash payment. Additionally, prior to the initiation of the research plan for each collaboration program, Bioverativ made a non-refundable payment of $1.4 million for the Sickle cell program and $2.8 million for the Hemophilia program as payment for the Company's services during the BV Bicycle Research Term. During the Joint Research Term, Bioverativ is obligated to fund a minimum of two FTE's based on an agreed upon FTE reimbursement rate and fund certain external costs incurred by the Company. Bioverativ has the option to obtain development and commercialization licenses associated with each designated collaboration product candidate in return for a fee of $5.0 million per drug candidate. In addition, Bioverativ would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, for each collaboration program, the Company is eligible to receive between $47.5 million and $67.0 million in development milestone payments for the Sickle Cell and Hemophilia programs, respectively, and up to $104.0 million in regulatory milestone payments for each program. In addition, the Company is eligible for up to $55.0 million in commercial milestone payments, on a research program by research program basis. Development milestone payments are triggered upon initiation of a defined phase of clinical research for a collaboration product. Regulatory milestone payments are triggered upon approval to market a product candidate by the FDA or other global regulatory authorities. Commercial milestone payments are triggered when an approved collaboration product reaches certain defined levels of net sales by the licensee. In addition, to the extent any of the collaboration products covered by the licenses conveyed to Bioverativ are commercialized, the Company would be entitled to receive tiered royalty payments of mid-single digits to low double digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including for instances where Bioverativ faces generic competition in certain countries. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from Bioverativ.

Under the terms of the Collaboration Agreement, Bioverativ was also provided with an option to obtain screening services on the additional Program 3 target upon making an option fee payment of $5.0 million in addition to a non-refundable payment of $1.4 million as payment for the Company's services related to Program 3 during the BV Bicycle Research Term. The option expired in November 2018 unexercised.

Either party may terminate the Bioverativ Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. Either party may terminate the Bioverativ Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. Bioverativ may terminate the Bioverativ Collaboration Agreement, entirely or on a program by program, licensed product by licensed product or country by country basis, for convenience upon not less than 30 days prior written notice to the Company.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

Accounting Analysis

The Company has identified the following four performance obligations associated with the Bioverativ Collaboration Agreement:

(i) Research License and the related research and development services during the BV Bicycle Research Term for Sickle cell program (the "Sickle Cell Research License and Related Services"),

(ii) Research License and the related research and development services during the BV Bicycle Research Term for Hemophilia program (the "Hemophilia Research License and Related Services"),

(iii) Material right associated with the sickle cell program development and exploitation license option ("Sickle Cell License Option Material Right"), and

(iv) Material right associated with the hemophilia program development and exploitation license option ("Hemophilia License Option Material Right").

The Company concluded that the option to obtain screening services on the additional Program 3 target is not a material right, as the option does not provide a discount that Bioverativ otherwise would not have received. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract. Research license and the related research and development services related to the Joint Research Term are not performance obligations at the inception of the arrangement, as they are optional services that will be performed if BioVerativ selects collaboration compounds for lead optimization. The amount paid by Bioverativ for the services during the Joint Research Team do not reflect a discount that the customer would otherwise receive and do not provide the customer with material rights.

The total transaction price was initially determined to be $14.2 million, consisting of the $10.0 million upfront payment and non-refundable research and development funding of $4.2 million. The Company may receive reimbursement of FTE costs and external costs associated with work under the Joint Research Term, milestone payments during the Joint Research Term, as well as upon exercise of the license options. These variable amounts are excluded from the transaction price as they relate to fees and milestones that can only be achieved subsequent to the exercise of an option.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the Research License and Related Services is primarily based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin what would be expected to be realized under similar contracts. The estimated standalone selling price for the material rights was determined based on the fees Bioverativ would pay to exercise the license options, the estimated value of the license option using comparable transactions, and the probability that the license options would be exercised by Bioverativ. Based on the relative standalone selling price, the allocation of the transaction price to

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

the separate performance obligations at the inception of the arrangement is as follows (in thousands):

Performance Obligations	Allocation of Transaction Price
Sickle Cell Research License and Related Services	$ 1,405
Hemophilia Research License and Related Services	2,811
Sickle Cell License Option Material Right	5,286
Hemophilia License Option Material Right	4,698
	$ 14,200

The Company will recognize revenue related to amounts allocated to the Sickle Cell and Hemophilia Research License and Related Services obligations as the underlying services are performed using a proportional performance model, over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent time expected, which best reflects the progress towards satisfaction of the performance obligation. The amount allocated to the material rights is recorded as deferred revenue and the Company will commence revenue recognition when the underlying option is exercised or upon expiry of the option.

During the three months ended March 31, 2019, Bioverativ extended the research and development services on both programs. The arrangement consideration increased to $14.7 million. On March 28, 2019, Bioverativ notified the Company that it would not exercise the Sickle Cell License Option. As a result, amounts allocated to the Sickle Cell License Option Material Right of $5.3 million were recognized into revenue during the three months ended March 31, 2019.

For the three months ended March 31, 2018 and 2019, the Company recognized $1.1 million and $6.0 million, respectively, of collaboration revenue related to its collaboration with Bioverativ. As of December 31, 2018 and March 31, 2019, the Company recorded deferred revenue of $9.9 million and $4.8 million, respectively, related to its collaboration with Bioverativ, respectively.

Oxurion Collaboration Agreement

Summary of Agreement

In August 2013, the Company entered into a Research Collaboration and License Agreement (the "Oxurion Collaboration Agreement") with Oxurion . Under the Oxurion Collaboration Agreement, the Company is responsible for identifying Bicycle peptides related to the collaboration target, plasma kallikrein, for use in various ophthalmic indications. Oxurion is responsible for further development and product commercialization after the defined research screening is performed by the Company.

Under the Oxurion Collaboration Agreement, the Company is obligated to perform specified research activities in accordance with the research plan, which includes two stages. Stage I, now completed, focused on the screening of targets using the Company's Bicycle peptide discovery platform with the goal of identifying compounds that meet the criteria set by the parties, and Stage II, now underway, during which Oxurion has continued research activities on selected Bicycle peptides with the goal of identifying compounds for further development and commercialization.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

The Company is not obligated or expected to perform any research services during Stage II of the research plan.

The Company granted certain worldwide intellectual property rights to Oxurion for the development, manufacture and commercialization of licensed compounds associated with plasma kallikrein. The Oxurion Collaboration Agreement provided for an upfront payment of €1.0 million and potential additional R&D funding, at an agreed upon FTE rate, should the research effort require more than one FTE or the research plan be amended or extended by Oxurion. In addition, Oxurion is required to make certain milestone payments to the Company upon the achievement of specified research, development, regulatory and commercial events. More specifically, for each collaboration program, the Company is eligible to receive up to €8.3 million in research and development milestones of which €1.8 million has been received as of March 31, 2019. In addition, the Company is eligible to receive up to €16.5 million upon achievement of certain regulatory milestone payments (e.g. €5 million for granting first regulatory approval in either the United States or EU for the first indication). In addition, to the extent any of the collaboration products covered by the licenses granted to Oxurion are commercialized, the Company would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from Oxurion.

Either party may terminate the Oxurion Collaboration Agreement if the other party has materially breached any of its material obligations and such breach continues after the specified cure period. Either party may terminate the Oxurion Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. Oxurion may terminate the Oxurion Collaboration Agreement, entirely or on a program by program, licensed product by licensed product or country by country basis, for convenience upon not less than 90 days prior written notice to the Company.

In November 2017, the parties executed the First Deed of Amendment to the Oxurion Collaboration Agreement ("First Amendment"). The First Amendment confirms that THR-149 has been selected as a development compound under the Oxurion Collaboration Agreement and that Stage II of the research plan has been completed. The First Amendment provided for additional research services to be performed by the Company related to the identification of two additional compounds for Oxurion, in its discretion, to select as development compounds. As for the work under the Oxurion Collaboration Agreement, the Company will perform the work under Stage I of the research plan which will be funded at a specified FTE rate, plus any direct out of pocket expenses, and Oxurion will be responsible for Stage II research and any development after the selection of a development compound. Additional milestones and royalties were added for the potential additional licensed compounds, consistent with those of the initial Oxurion Collaboration Agreement. The Company is not obligated or expected to perform any research services during Stage II of the research plan.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

Accounting Analysis

Under the Oxurion Collaboration Agreement, all licenses were granted and research services to be provided by the Company were fully completed and revenue associated with those obligations was fully recognized prior to January 1, 2016. Under the First Amendment, the Company has identified a single performance obligation associated with the performance of research services associated with Stage I of the research plan for which the Company will be reimbursed for its services at a specified FTE reimbursement rate plus out of pocket costs which will be recognized on a proportional performance basis as the associated FTE efforts and costs are incurred, which best reflects the progress towards satisfaction of the performance obligation. None of the unpaid development or regulatory milestones have been included in the transaction price, as all milestone are not considered probable at December 31, 2018 and March 31, 2019.

For the three months ended March 31, 2018 and 2019, the Company recognized $1.4 million and $0.0 million, respectively, of revenue related to its agreements with Oxurion. As of March 31, 2019, the research services under the First Amendment were complete. The revenue recognized for the three months ended March 31, 2018 and 2019 includes $1.2 million and $0.0 million, respectively, related to the achievement of developmental milestones during the advancement of the research by Oxurion into a Phase I clinical study. There was no deferred revenue recorded as of December 31, 2018 and March 31, 2019 in connection with the agreements with Oxurion.

Summary of Contract Assets and Liabilities

Up-front payments and fees are recorded as deferred revenue upon receipt or when due until such time as the Company satisfies its performance obligations under these arrangements. A contract asset is a conditional right to consideration in exchange for goods or services that the Company has transferred to a customer. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

The following table presents changes in the balances of the Company's contract assets and liabilities (in thousands):

	Balance at Beginning of Year	Additions	Deductions	Impact of Exchange Rates	Balance at End of Period
Period ended December 31, 2018					
Contract assets	$ —	$ 91	$ (91)	$ —	$ —
Contract liabilities:					
Deferred revenue					
Bioverativ collaboration deferred revenue	14,467	—	(4,006)	(553)	9,908
AstraZeneca collaboration deferred revenue	—	5,350	(466)	(157)	4,727
Total deferred revenue	$ 14,467	$ 5,350	$ (4,472)	$ (710)	$ 14,635

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

	Balance at Beginning of Period	Additions	Deductions	Impact of Exchange Rates	Balance at End of Period
Period ended March 31, 2019					
Contract assets	$ —	$ —	$ —	$ —	$ —
Contract liabilities:					
Deferred revenue					
Bioverativ collaboration deferred revenue	9,908	—	(5,286)	144	4,766
AstraZeneca collaboration deferred revenue	4,727	24	(10)	97	4,838
Total deferred revenue	$ 14,635	$ 24	$ (5,295)	$ 240	$ 9,604

The contract assets represents research and development services which have been performed but have not yet been billed, and are reduced when they are subsequently billed.

The Bioverativ deferred revenue balance at March 31, 2019 is comprised of $4.8 million allocated to the Hemophilia License Option Material Right, which will commence revenue recognition when the respective option is exercised at the end of Joint Research Term or when the option expires.

The AstraZeneca deferred revenue balance at March 31, 2019 includes $4.7 million allocated to the Target 3, Target 4, Target 5 and Target 6 Material Rights, which will commence revenue recognition when the respective option is exercised at the end of AZ Research Term or when the option expires. The remaining balance relates to research and development services billed in advance that will be recognized over the Bicycle Research Term.

During the three months ended March 31, 2018 and 2019, the Company recognized the following revenues as a result of changes in the contract asset and the contract liability balances in the respective periods (in thousands):

	Three Months Ended March 31,	
	2018	2019
Revenue recognized in the period from:		
Revenue recognized based on proportional performance	$ (1,118)	$ (5,295)

Cancer Research UK

On December 13, 2016, the Company entered into a Clinical Trial and License Agreement with Cancer Research Technology Limited ("CRTL") and Cancer Research UK ("CRUK"). Pursuant to the agreement, as amended in March 2017 and June 2018, CRUK's Centre for Drug Development will sponsor and fund a Phase Ia and Phase IIa clinical trial for the Company's lead product candidate, BT1718, a Bicycle Toxin Conjugate, in patients with advanced solid tumors.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

CRUK is responsible to design, prepare, carry out and sponsor the clinical trial at its cost. The Company is responsible for supplying agreed quantities of GMP materials for the study, the supply of which has been completed. In the event that additional quantities are needed, the Company will provide CRUK with all reasonable assistance to complete the arrangements necessary for the generation and supply of such additional GMP materials but CRUK will be responsible for supplying and paying for such additional quantities of GMP materials.

The Company granted CRUK a license to its and its affiliates' intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial the Company retains the right to continue the development of BT1718 during the clinical trial. Upon the completion of the Phase I/IIa clinical study, the Company has the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and the Company decides to abandon development of all products that deliver cytotoxic payloads to the MT1 target antigen, the Company will assign or grant to CRTL an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case the Company will receive a mid to high double digit percentage of the net revenue depending on the stage of development when the license is granted). The CRUK agreement contains additional future milestone payments upon the achievement of development and regulatory milestones, payable in cash and shares, with an aggregate total value of $50.9 million, as well as royalty payments based on a high double digit percentage on net sales of products developed.

The CRUK agreement can be terminated by either party upon an insolvency event, material breach of the terms of the contract, or upon a change in control (and the new controlling entity generates its revenue from the sale of tobacco products or is an affiliate of such party). CRUK may terminate the arrangement for safety reasons or if it determines that the objectives of the clinical trial will not be met, in which case, if the study is terminated by CRUK prior to the completion of the Phase 1a dose escalation portion of the study for such reasons or if CRUK refuses release of any additional quantities of GMP materials or if the parties cannot agree upon a plan to supply the additional quantities of GMP materials, the Company will be obligated to refund fifty percent of the costs and expenses incurred or committed by CRUK to perform the clinical trial. If the study is terminated by CRUK for an insolvency event, a material breach by the Company, or if the Company is acquired by an entity that generates its revenue from the sale of tobacco products or is an affiliate of such party, the Company will reimburse CRUK in full for all costs paid or committed in connection with the clinical trial and no further license payments, where applicable, shall be due. In such case where we are acquired by an entity that generates its revenue from the sale of tobacco products or is an affiliate of such party, CRUK will not be obliged to grant a license to the Company in respect of the results of the clinical trial and the Company will assign or grant to CRT an exclusive license to develop and commercialize the product without CRT being required to make any payment to the Company.

The Company concluded that the costs incurred by CRUK is a liability in accordance with ASC 730, Research and Development, as the payment is not based solely on the results of the research and development having future economic benefit. As such, the Company recorded a liability of $0.8 million and $1.0 million at December 31, 2018 and March 31, 2019, respectively, which is recorded in other long-term liabilities in the consolidated balance sheets. The liability is

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

10. Significant Agreements (Continued)

recorded as incremental research and development expense in the statements of operations and comprehensive loss.

11. Income Taxes

The components of net loss before tax provision from income taxes are as follows (in thousands):

	Three Months Ended March 31,	
	2018	2019
United Kingdom	$ (2,901)	$ (6,397)
United States	(29)	(26)
Total	$ (2,930)	$ (6,423)

The components of the benefit for income taxes are as follows (in thousands):

	Three Months Ended March 31,	
	2018	2019
Current income tax provision (benefit)		
Federal	$ (13)	$ (2)
State	15	(1)
Total current income tax provision (benefit)	2	(3)
Deferred income tax provision (benefit)		
Federal	(179)	58
State	(219)	25
Total deferred income tax provision (benefit)	(398)	83
Total provision for (benefit from) income taxes	$ (396)	$ 80

A reconciliation of the provision (benefit) for income taxes computed at the statutory income tax rate to the provision (benefit) for income taxes as reflected in the financial statement is as follows:

	Three Months Ended March 31,	
	2018	2019
Provision (benefit) for income taxes at statutory rate	19%	19%
(Decreases) increases resulting from:		
Federal tax credits	1.1%	1.0%
Change in valuation allowance	(7.2)%	(6.7)%
Net losses surrendered for research credit	(3.7)%	(4.9)%
Preferred share warrants	(0.6)%	(2.2)%
Other	4.9%	(7.5)%
Effective income tax rate	13.5%	(1.3)%

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

11. Income Taxes (Continued)

During the three months ended March 31, 2018, the Company recorded an income tax benefit of $0.4 million. During the three months ended March 31, 2019, the Company recorded an income tax provision of $0.1 million. The Company is subject to United Kingdom corporate taxation. Due to the nature of its business, the Company has generated losses since inception and has therefore not paid United Kingdom corporation tax. The Company's income tax benefit is mainly the result of deferred tax assets benefitted in the United States that do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement. The Company's income tax provision recognized represents income tax payable in the United States on profits generated from an intercompany service arrangement.

The Company regularly assesses its ability to realize its deferred tax assets. Assessing the realization of deferred tax assets requires significant judgment. In determining whether its deferred tax assets are more likely than not realizable, the Company evaluated all available positive and negative evidence, and weighed the evidence based on its objectivity. After consideration of the evidence, including the Company's history of cumulative net losses in the U.K., and has concluded that it is more likely than not that the Company will not realize the benefits of its U.K. deferred tax assets and accordingly the Company has provided a valuation allowance for the full amount of the net deferred tax assets in the U.K. The Company has considered the Company's history of cumulative net profits in the United states, estimated future taxable income and concluded that it is more likely than not that the Company will realize the benefits of its United State deferred tax assets and has not provided a valuation allowance against the net deferred tax assets in the United States. The change in the valuation allowance in the three months ended March 31, 2019 was immaterial.

The Company recorded a valuation allowance against all of its U.K. deferred tax assets as of December 31, 2018 and March 31, 2019.

The Company intends to continue to maintain a full valuation allowance on its U.K. deferred tax assets until there is sufficient evidence to support the reversal of all or some portion of these allowances. The release of the valuation allowance would result in the recognition of certain deferred tax assets and an increase to the benefit for income taxes for the period the release is recorded. However, the exact timing and amount of the valuation allowance release are subject to change on the basis of the level of profitability that the Company is able to actually achieve.

The benefit for income taxes shown on the consolidated statements of operations differs from amounts that would result from applying the statutory tax rates to income before taxes primarily because of certain permanent expenses that were not deductible, U.K., federal and state research and development credits, as well as the application of valuation allowances against the U.K. deferred tax assets.

As of December 31, 2018, the Company had $29.1 million of U.K. operating loss carryforwards and $0 of federal and state net operating loss carryforwards. As of March 31, 2019, the Company had $40.5 million of U.K. operating loss carryforwards and $0 of U.S. federal and state net operating loss carryforwards. The U.K. operating loss carryforwards have an indefinite life. As of March 31, 2019, the Company had $0.2 and $0.4 million of federal and state research and development credit carryforwards, respectively, that expire at various dates through 2038.

The Company recognizes, in its consolidated financial statements, the effect of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

11. Income Taxes (Continued)

upon examination. The Company had no uncertain tax positions during the year ended of December 31, 2018 or the three months ended March 31, 2019. There are no amounts of interest or penalties recognized in the consolidated statement of operations or accrued on the consolidated balance sheet for any period presented. The Company does not expect any material changes in these uncertain tax benefits within the next 12 months.

The Company files income tax returns in the United Kingdom, and in the United States for federal income taxes and in the Commonwealth of Massachusetts for state income taxes. In the normal course of business, the Company is subject to examination by tax authorities in these jurisdictions. The 2017 tax year remains open to examination the by HM Revenue & Customs. The statute of limitations for assessment with the Internal Revenue Service is generally three years from filing the tax return. As such, all years since inception in the U.S. remain open to examination. The Company is currently not under examination by jurisdictions for any tax years.

12. Commitments and Contingencies

Leases

In September 2015, the Company entered into a tenancy agreement for space in Building 260 Babraham Research Campus, Cambridge, UK for a period of two years, beginning on October 1, 2015. The annual rent was approximately $0.2 million plus service charges. In October 2017 this agreement was extended until January 2018 with annual rent of approximately $0.2 million.

In September 2017, Bicycle Therapeutics Inc. entered into a lease agreement for office and laboratory space in Lexington, Massachusetts, which commenced on January 1, 2018 and expires on December 31, 2022. Bicycle Therapeutics Inc. has the option to extend for a successive period which is not included in the lease term as it is not reasonably certain that the option will be exercised. In conjunction with the lease agreement, Bicycle Therapeutics Inc. paid a security deposit of $0.2 million as well as prepaid rent of $0.1 million for the first month of the third, fourth, and fifth year of the lease. The deposit is recorded in other assets in the consolidated balance sheets. With the adoption of ASU 2016-02, the Company has recorded a right-of-use asset (inclusive of the impact of prepaid rent) and corresponding lease liability, by calculating the present value of lease payments, discounted at 9%, the incremental borrowing rate, over the lease term.

In October 2017, the Company entered into a lease agreement for office and laboratory space in Building 900, Babraham Research Campus, Cambridge, U.K., which expires on December 21, 2021. The annual rent is approximately $0.5 million. The Company has the right to renew the lease for five years commencing December 21, 2021, which is not included in the lease term as it is not reasonably certain that the right will be exercised. Service charges are also payable based on floor area and are estimated to be approximately $0.1 million per year. In conjunction with the lease agreement, the Company paid a security deposit of $0.6 million, which is recorded in other assets in the consolidated balance sheets. With the adoption of ASC 2016-02, the Company has recorded a right-of-use asset and corresponding lease liability, by calculating the present value of lease payments, discounted at 7.75%, the incremental borrowing rate, over the lease term.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

The future minimum lease payments due under the Company's operating leases as of December 31, 2018 were as follows (in thousands):

Year Ending December 31,	
2019	888
2020	901
2021	915
2022	483
2023	—
	$ 3,187

Prior to the adoption of ASU 2016-02 and for the three months ended March 31, 2018, the Company recognized rent expense on a straight-line basis over the lease period and recorded deferred rent for rent expense incurred but not yet paid. During the three months ended March 31, 2018, the Company recognized total rent expense of $0.3 million.

The Company identified and assessed the following significant assumptions in recognizing the right-of-use assets and corresponding lease liabilities:

- *Expected lease term* — The expected lease term includes both contractual lease periods and, when applicable, cancelable option periods when it is reasonably certain that the Company would exercise such options. The Company has not included any option periods in the expected lease term as it is not reasonably certain that the Company will exercise such options.

- *Incremental borrowing rate* — The Company's lease agreements do not provide an implicit rate. As the Company does not have any external borrowings for comparable terms of its leases, the Company estimated the incremental borrowing rate by comparing interest rates available in the market for similar borrowings and third-party quotations.

- *Lease and non-lease components* — In certain cases, the Company is also responsible for certain additional charges for operating costs, including insurance, maintenance, taxes, and other costs incurred, which are billed based on both usage and as a percentage of the Company's share of total squared footage. The amounts paid are considered non-lease components. The Company has elected the practical expedient which allows the non-lease components to be combined with the lease components. The payments for other operating costs are considered variable lease cost and are recognized in the period in which the costs are incurred.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

The components of the Company's lease expense, which are recorded as a component of research and development expenses and general and administrative expenses in the unaudited consolidated statement of operations are as follows (in thousands):

	Three Months Ended March 31, 2019
Operating lease cost	$ 224
Variable lease cost	87
Total lease cost	$ 311
Weighted-average remaining operating lease term (years)	3.3
Weighted-average discount rate	8.48%

The following table summarizes the maturities of the Company's operating leases as of March 31, 2019 (in thousands):

Year Ending December 31,	
2019	$ 673
2020	873
2021	772
2022	443
2023	—
Present value adjustment	(340)
Total lease liabilities	$ 2,421
Less: current lease liabilities	(584)
Long term lease liabilities	$ 1,837

The Company has entered into various agreements with contract manufacturing organizations to provide clinical trial materials and with vendors for preclinical research studies, synthetic chemistry and other services for operating purposes. These payments are not included in the table of operating lease payments above since the contracts are generally cancelable at any time upon less than 90 days' prior written notice. The Company is not contractually able to terminate for convenience and avoid any and all future obligations to these vendors. Under such agreements, the Company is contractually obligated to make certain minimum payments to the vendors, with the payments in the event of a termination with less than 90 days' notice based on the timing of the termination and the exact terms of the agreement.

Legal proceedings

From time to time, the Company or its subsidiaries may become involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

In September 2016, the Company filed a complaint in the District Court of the Hague against Pepscan Systems B.V. ("Pepscan") to contest the right of Pepscan to terminate a non-exclusive patent license agreement we entered into with Pepscan in 2009 and 2010 ("PLA"). In response, Pepscan counterclaimed for injunctive relief and unquantified damages. The Company is vigorously prosecuting its claims and defending against those of Pepscan. The Company does not believe that a loss is probable or estimable at this time, and as such, the Company has not recorded a liability related to the Pepscan litigation as December 31, 2018 or at March 31, 2019. Should the Company not be successful in maintaining its rights to Pepscan's patent or in the Company's alternative demand that the patent be invalidated, commercialization of the Company's lead product could be delayed. As the Pepscan patent expires prior to the expected commercialization date of the product, the Company does not believe that the legal proceedings could have a material adverse effect on the Company's business and operating results.

Founder Royalty arrangements

At the time BicycleRD Limited was organized, BicycleRD Limited entered into a royalty agreement with its founders and initial investors (the "Founder Royalty Agreement"). Pursuant to the Founder Royalty Agreement, the Company will pay a royalty rate in the low single digit percentages on net product sales to its founders and initial investors, for a period of 10 years from the first commercial sale on a country by country basis. No royalties have been earned or paid under the royalty arrangements to date.

In accordance with the terms of the Founder Royalty Agreements, as amended in May 2017, the parties amended the terms of the royalty arrangements to limit the future royalties payments to net sales on future products that could be generated under the collaboration with Oxurion and AstraZeneca, in exchange for the issuance of warrants to subscribe for 200,000 Series A Preferred Shares.

Indemnification obligations

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has indemnification obligations towards members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification arrangements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnification obligations. The Company is not aware of any claims under indemnification arrangements, and therefore it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2018 and March 31, 2019.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

13. Net loss and unaudited pro forma net loss per share

Net loss per share

Basic and diluted net loss per share attributable to ordinary shareholders was calculated as follows (in thousands, except share and per share amounts):

	Three Months Ended March 31,	
	2018	2019
Numerator:		
Net loss attributable to ordinary shareholders	$ (2,534)	$ (6,503)
Denominator:		
Weighted average ordinary shares outstanding, basic and diluted	397,483	834,043
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (6.38)	$ (7.80)

The Company's potentially dilutive securities, which include share options, convertible preferred shares and warrants to subscribe for Series A and Series B1 Preferred Shares, and unvested restricted shares, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of ordinary shares outstanding used to calculate both basic and diluted net loss per share attributable to ordinary shareholders is the same. The Company excluded the following potentially dilutive ordinary shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to ordinary shareholders for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended March 31,	
	2018	2019
Convertible preferred shares (as converted to ordinary shares)	9,641,740	11,647,529
Warrants to subscribe for convertible preferred shares (as adjusted to reflect the impact of the share capital reorganization and issuance of bonus shares (Note 1))[(1)]	1,347,953	1,347,953
Restricted ordinary shares	126,740	56,643
Options to purchase ordinary shares	976,319	930,861
	12,092,752	13,982,972

(1) On March 7, 2019, the holders of the Series B1 warrants to subscribe for Series B1 Preferred Shares agreed that 50% of the warrants will be exercised in conjunction with the IPO and 50% of the warrants will expire.

Unaudited pro forma net loss per share attributable to ordinary shareholders

The unaudited pro forma basic and diluted net loss per share attributable to ordinary shareholders for the three months ended March 31, 2019 have been prepared to give effect to adjustments arising upon the completion of the proposed IPO as if the IPO had occurred on January 1, 2019. The unaudited pro forma net loss attributable to ordinary shareholders used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to ordinary

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

13. Net loss and unaudited pro forma net loss per share (Continued)

shareholders does not include the effects the change in fair value of the warrant liability because the calculation gives effect to (i) the conversion of all outstanding convertible preferred shares into ordinary shares upon the completion of an IPO and (ii) the exercise of 200,000 warrants to subscribe for Series A convertible preferred shares immediately prior to an IPO, and (iii) the exercise of the warrants to subscribe for 371,645 Series B1 convertible preferred shares (Note 7), as if the proposed IPO had occurred on the later of January 1, 2019 or the issuance date of the convertible preferred shares and the warrants to subscribe for convertible preferred shares.

	Three Months Ended March 31, 2019
Numerator:	
Net loss attributable to ordinary shareholders	$ (6,503)
Change in fair value of preferred stock warrant liability	3,197
Pro forma net loss attributable to ordinary shareholders	$ (3,306)
Denominator:	
Weighted average ordinary shares outstanding, basic and diluted	834,043
Pro forma adjustment to reflect the weighted average conversion of all outstanding convertible preferred shares into ordinary shares upon the completion of an IPO	11,642,480
Pro forma adjustment to reflect the exercise of warrants to subscribe for convertible preferred shares which expire upon the completion of an IPO as adjusted to reflect the impact of the share recapitalization and issuance of bonus shares (Note 1)	816,877
Pro forma weighted average ordinary shares outstanding, basic and diluted	13,293,400
Pro forma net loss per share attributable to ordinary shareholders, basic and diluted	$ (0.25)

14. Benefit plans

The Company established a defined-contribution savings plan under Section 401(k) of the Code (the "401(k) Plan"). The 401(k) Plan covers all U.S. employees and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the 401(k) Plan may be made at the discretion of the Company's board of directors. During the three months ended March 31, 2018 and 2019 the Company made contributions totaling $0.1 million and $0.1 million, respectively, to the 401(k) Plan.

The Company provides a pension contribution plan for its employees in the United Kingdom, pursuant to which the Company may match employees contributions each year ("U.K Plan"). During the three months ended March 31, 2018 and 2019 the Company made contributions totaling $0.1 million and $0.1 million, respectively, to the U.K. Plan.

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

15. Related party transactions

The Company has entered into Founder Royalty Agreements with its founders and initial investors (Note 12). No royalties have been earned or paid under the Founder Royalty Agreements to date.

The former Chairman of the Company's Board of Directors is associated with 10X Capital Inc., who provided consultancy services to the Company totaling $25,000 and $50,000 a during the three months ended March 31, 2018 and 2019, respectively.

16. Geographic information

The Company operates in two geographic regions: the United States and the United Kingdom. Information about the Company's long-lived assets, including operating lease right-of-use assets, held in different geographic regions is presented in the table below (in thousands):

	December 31, 2018	March 31, 2019
United States	$ 498	$ 1,961
United Kingdom	1,320	2,428
	$ 1,818	$ 4,389

The Company's collaboration revenues are attributed to the operations of the Company in the United Kingdom.

17. Subsequent events

The Company evaluated subsequent events through May 13, 2019, the date on which those financial statements were issued, noting none that are material the Company's financial statements.

In May 2019, we entered into a collaboration with the Dementia Discovery Fund, or DDF, to use Bicycle technology for the discovery and development of novel therapeutics for dementia. Under the terms of the agreement, Bicycle and DDF will collaborate to identify Bicycles that bind to clinically validated dementia targets. The Company will receive $1.1 million within 15 days of the execution of the arrangement, and may receive up to an additional $0.7 million upon the achievement of certain milestones. If promising lead compounds are identified, DDF and Bicycle have the option to establish a jointly-owned new company with Bicycle to advance the compounds through further development towards commercialization. The jointly-owned company will receive a royalty and milestone-bearing assignment and license of intellectual property from Bicycle for this purpose.

On May 9, 2019, the Company's board of directors and shareholders approved the following corporate actions:

- the reorganization of the Company's share capital, effective on May 13, 2019, by issuing ordinary shares as bonus shares to each holder of ordinary shares on the basis of 1.429 bonus shares for each ordinary share in issue (having the effect of a one for 1.429 share split without having an impact on the nominal value of the ordinary shares);

Bicycle Therapeutics Limited

Notes to Unaudited Consolidated Financial Statements (Continued)

17. Subsequent events (Continued)

- upon the closing of a firm commitment underwritten public offering in which the aggregate proceeds raised in the offering equal or exceed $50 million, the Company's Series A and Series B1 Preferred Shares and Series B2 Preferred Shares will be automatically converted into ordinary shares at the applicable conversion price adjusted accordingly for the share split;

- the authorized number of ordinary shares was increased from 15,452,420 to 31,995,653;

- the adoption of the 2019 Share Option and Incentive plan, or the 2019 Plan, which will become effective immediately prior to the effectiveness of the registration statement on Form S-1 related to the Company's initial public offering. The 2019 Plan provides for the grant of options to purchase ordinary shares, share appreciation rights, restricted shares, restricted share units, and other share-based awards, and 2,470,583 additional ordinary shares are reserved under the 2019 Plan;

- the adoption of the 2019 Employee Share Purchase Plan, which will become effective upon the closing of the Company's initial public offering. An additional 215,000 ordinary shares will become available for future issuance under this plan;

- the authorization for management to re-register the Company as a public company limited by shares with the name Bicycle Therapeutics Plc.

4,333,333 American Depositary Shares

Representing 4,333,333 Ordinary Shares

Goldman Sachs & Co. LLC **Jefferies** **Piper Jaffray**

Canaccord Genuity

Through and including , 2019 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

PART II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses, other than underwriting discounts and commissions, which are expected to be incurred in connection with our sale of ADSs in this offering. With the exception of the registration fee payable to the SEC, the Nasdaq listing fee and the filing fee payable to FINRA, all amounts are estimates.

SEC registration fee	$	10,454
FINRA filing fee		13,437
Nasdaq listing fee		125,000
Printing and engraving expenses		55,000
Legal fees and expenses		1,985,000
Accounting fees and expenses		1,131,000
Miscellaneous fees and expenses		50,109
Total	$	3,370,000

Item 14. Indemnification of Directors and Officers.

Subject to the Companies Act, members of the registrant's board of directors and its officers (excluding auditors) have the benefit of the following indemnification provisions in the registrant's Articles of Association:

Current and former members of the registrant's board of directors or officers shall be reimbursed for:

(i) all costs, charges, losses, expenses and liabilities sustained or incurred in relation to his or her actual or purported execution of his or her duties in relation to the registrant, including any liability incurred in defending any criminal or civil proceedings; and

(ii) expenses incurred or to be incurred in defending any criminal or civil proceedings, in an investigation by a regulatory authority or against a proposed action to be taken by a regulatory authority, or in connection with any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the registrant as a company, or collectively the Statutes, arising in relation to the registrant or an associated company, by virtue of the actual or purposed execution of the duties of his or her office or the exercise of his or her powers.

In the case of current or former members of the registrant's board of directors, there shall be no entitlement to reimbursement as referred to above for (i) any liability incurred to the registrant or any associated company, (ii) the payment of a fine imposed in any criminal proceeding or a penalty imposed by a regulatory authority for non-compliance with any requirement of a regulatory nature, (iii) the defense of any criminal proceeding if the member of the registrant's board of directors is convicted, (iv) the defense of any civil proceeding brought by the registrant or an associated company in which judgment is given against the director and (v) any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the registrant as a company in which the court refuses to grant relief to the director.

In addition, members of the registrant's board of directors and its officers who have received payment from the registrant under these indemnification provisions must repay the amount they received in accordance with the Statutes or in any other circumstances that the registrant may prescribe or where the registrant has reserved the right to require repayment.

The underwriting agreement the registrant will enter into in connection with the offering of ADSs being registered hereby provides that the underwriters will indemnify, under certain conditions, the registrant's board of directors and its officers against certain liabilities arising in connection with this offering.

Item 15. Recent Sales of Unregistered Securities.

In the three years preceding the filing of this Registration Statement, we have issued the following securities that were not registered under the Securities Act:

(a) Issuances of Share Capital

On October 3, 2016, we issued 406,001 Series A preferred shares to seven investors for an aggregate subscription price of £4,060,010.

On May 26, 2017, we issued warrants to subscribe for up to 200,000 Series A preferred shares to five investors with an exercise price of £0.01 per share.

On May 26, 2017, we issued 3,562,583 Series B1 preferred shares to eight investors for an aggregate subscription price of £39,999,969.41.

On May 26, 2017 we issued warrants to subscribe for up to 627,903 Series B1 preferred shares to three investors with an exercise price of £0.01 per share.

On October 27, 2017, we issued 384,615 Series B1 preferred shares to one investor for an aggregate subscription price of £4,999,995.

On October 27, 2017, we issued warrants to subscribe for up to 115,384 Series B1 preferred shares to a new unaffiliated investor with an exercise price of £0.01 per share.

On December 17, 2018, we issued 251,904 ordinary shares to existing employees for an aggregate of £2,519.04.

On December 20, 2018, we issued 1,323,248 Series B2 preferred shares to three investors for an aggregate subscription price of £20,576,506.40.

On January 3, 2019, we issued 80,385 Series B2 preferred shares to one investor for an aggregate subscription price of £1,249,986.75.

The sales of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering, or pursuant to Regulation S promulgated under the Securities Act in that offers, sales and issuances were not made to persons in the United States and no directed selling efforts were made in the United States. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

(b) Grants and Exercises of Options and Restricted Share Awards

From April 2016 to the date of the prospectus that forms a part of this registration statement, we issued share options to subscribe for an aggregate of 1,573,345 ordinary shares, with exercise prices ranging from £0.01 to £6.37 per ordinary share, to employees and directors.

From April 2016 to the date of the prospectus that forms a part of this registration statement, we issued 61,295 ordinary shares to individuals upon exercise of options for an aggregate subscription price of £16,945.47.

From April 2016 to the date of the prospectus that forms a part of this registration statement, we issued 576,350 ordinary shares to individuals pursuant to share vesting agreements, for an aggregate subscription price of £4,033.33.

The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans, or pursuant to Regulation S promulgated under the Securities Act in that offers, sales and issuances were not made to persons in the United States and no directed selling efforts were made in the United States. The ordinary shares issued upon the exercise of options are deemed to be restricted securities for purposes of the Securities Act.

All certificates representing the securities issued in the transactions described in this Item 15 included appropriate legends setting forth that the securities had not been offered or sold pursuant to a registration statement and describing the applicable restrictions on transfer of the securities. There were no underwriters employed in connection with any of the transactions set forth in this Item 15.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits:

Exhibit number	Description of exhibit
1.1	Form of Underwriting Agreement.
3.1	Articles of Association of Bicycle Therapeutics Limited, as currently in effect.
3.2	Form of Articles of Association of the registrant (to be effective upon the closing of this offering).
4.1	Form of Deposit Agreement.
4.2	Form of American Depositary Receipt (included in Exhibit 4.1).
5.1	Opinion of Goodwin Procter (UK) LLP.
10.1*	Registration Rights Agreement by and among Bicycle Therapeutics Limited and the Investors listed therein, dated December 21, 2018.
10.2#*	Form of Share Option Contract of Bicycle Therapeutics Limited for employees in England.
10.3#*	Form of Share Option Contract of Bicycle Therapeutics Limited for employees in the United States.
10.4#	Senior Executive Cash Incentive Bonus Plan.
10.5#	2019 Employee Share Purchase Plan.
10.6#	2019 Share Option Plan and forms of award agreements thereunder (to be adopted prior to the effectiveness of this registration statement).
10.7#**	Employment Agreement between the registrant and Kevin Lee, Ph.D., MBA, to be in effect upon the closing of this offering.

Exhibit number	Description of exhibit
10.8#**	Employment Agreement between the registrant and Lee Kalowski, MBA, to be in effect upon the closing of this offering.
10.9#**	Employment Agreement between the registrant and Michael Skynner, Ph.D., to be in effect upon the closing of this offering.
10.10#**	Employment Agreement between the registrant and Nicholas Keen, Ph.D., to be in effect upon the closing of this offering.
10.11#**	Employment Agreement between the registrant and Peter Leone, MBA, dated January 28, 2019.
10.12#	Form of Deed of Indemnity between the registrant and each of its directors and executive officers.
10.13	Contract for the Sale of Leasehold Land with Vacant Possession, by and between Convergence Pharmaceuticals Limited and BicycleRD Limited, dated October 31, 2017, which is pursuant to the Underlease of Ground and First Floor Premises Building 900 Babraham Research Campus Babraham Cambridge, between Imperial College Thinkspace Limited, Convergence Pharmaceuticals Limited and Biogen Idec Limited, dated March 2, 2017.
10.14*	Lease Agreement, by and between Bicycle Therapeutics Inc. and King 4 Hartwell Place, LLC, dated September 26, 2017.
10.15+*	Clinical Trial and License Agreement, by and between Bicycle Therapeutics Limited, Cancer Research Technology Limited, and Cancer Research UK, dated December 13, 2016, as amended and restated by the Deed of Amendment on March 31, 2017, as further amended by the Second Deed of Amendment on June 29, 2018.
21.1*	Subsidiaries of the registrant.
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
23.2	Consent of Goodwin Procter (UK) LLP (included in Exhibit 5.1).
24.1*	Power of Attorney.
99.1	Consent of Director Nominee.

* Previously filed.

** To be filed by amendment.

# Indicates a management contract or any compensatory plan, contract or arrangement.

\+ Confidential treatment has been requested for portions of this exhibit. These portions have been omitted from the registration statement and filed separately with the United States Securities and Exchange Commission.

(b) Financial Statements Schedules:

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Act, may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is therefore unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The Registrant hereby undertakes that:

(a) The Registrant will provide to the underwriter at the closing as specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

(b) For purposes of determining any liability under the Securities Act of 1933, as amended, the information omitted from a form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933, as amended, shall be deemed to be part of this registration statement as of the time it was declared effective.

(c) For the purpose of determining any liability under the Securities Act of 1933, as amended, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, under the laws and regulations of England and Wales, on May 13, 2019.

BICYCLE THERAPEUTICS LIMITED

By: /s/ KEVIN LEE

Name: Kevin Lee, Ph.D., MBA
Title: *Chief Executive Officer*

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ KEVIN LEE Kevin Lee, Ph.D., MBA	Chief Executive Officer and Director (Principal Executive Officer)	May 13, 2019
/s/ LEE KALOWSKI Lee Kalowski, MBA	Chief Financial Officer and President (Principal Financial and Accounting Officer)	May 13, 2019
* Pierre Legault, MBA, CPA	Chairman and Director	May 13, 2019
* Michael Anstey, DPhil	Director	May 13, 2019
* Catherine Bingham, MBA	Director	May 13, 2019
* Deborah Harland, Ph.D., MBA	Director	May 13, 2019
* Anja König, Ph.D.	Director	May 13, 2019

Signature	Title	Date
*		
Eashwar Krishnan	Director	May 13, 2019
*		
Carolyn Ng, Ph.D.	Director	May 13, 2019
*		
Jason Rhodes, MBA	Director	May 13, 2019
*		
Sir Gregory Winter, FRS	Director	May 13, 2019
*		
Lee Kalowski, MBA	Authorized Representative in the United States	May 13, 2019

*By: /s/ LEE KALOWSKI

Name: Lee Kalowski
Title: *Attorney-in-fact*

Exhibit 1.1

Bicycle Therapeutics plc

[·] American Depositary Shares representing

[·] Ordinary Shares, nominal value £0.01 per share

Underwriting Agreement

[·], 2019

Goldman Sachs & Co. LLC
Jefferies LLC
Piper Jaffray & Co.

As representatives (the "Representatives") of the several Underwriters
named in Schedule I hereto

c/o Goldman Sachs & Co. LLC
200 West Street
New York, NY 10282-2198

c/o Jefferies LLC
520 Madison Avenue
New York, NY 10022

c/o Piper Jaffray & Co.
345 Park Avenue, 12th Floor
New York, NY 10154

Ladies and Gentlemen:

Bicycle Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the "Company"), proposes, subject to the terms and conditions stated in this agreement (this "Agreement"), and in the manner contemplated by the Agreement, to issue and sell to the several Underwriters named in Schedule I hereto (the "Underwriters") for whom you are acting as representatives (the "Representatives") an aggregate of [·] American Depositary Shares representing [·] Ordinary Shares nominal value £0.01 per share (the "Ordinary Shares") and, at the election of the Underwriters, up to [·] additional American Depositary Shares representing [·] Ordinary Shares. The aggregate of [·] American Depositary Shares representing [·] Ordinary Shares to be sold by the Company is herein called the "Firm ADSs", and the aggregate of [·] American Depositary Shares representing [·] additional Ordinary Shares to be sold by the Company is called the "Optional ADSs". The Firm ADSs and the Optional ADSs that the Underwriters elect to purchase pursuant to Section 2 hereof are collectively called the "ADSs". The Ordinary Shares represented by the Firm

ADSs are hereinafter called the "Firm Shares" and the Ordinary Shares represented by the Optional ADSs are hereinafter called the "Optional Shares", and the Firm Shares and the Optional Shares are herein collectively called the "Shares". The ADSs together with the Shares are herein collectively called the "Offered Securities".

The ADSs are to be issued pursuant to a deposit agreement (the "Deposit Agreement"), dated as of [·], 2019, among the Company, Citibank, N.A., as depositary (the "Depositary"), and the holders and beneficial owners from time to time of the American Depositary Receipts (the "ADRs") issued thereunder by the Depositary and evidencing the ADSs. Each ADS will initially represent the right to receive [·] Ordinary Shares deposited pursuant to the Deposit Agreement.

1. The Company represents and warrants to, and agrees with, each of the Underwriters that:

(a) A registration statement on Form S-1 (File No. 333–231076) (the "Initial Registration Statement") in respect of the Offered Securities has been filed with the Securities and Exchange Commission (the "Commission"); the Initial Registration Statement and any post-effective amendments thereto, each in the form heretofore delivered to you, have been declared effective by the Commission in such form; other than a registration statement, if any, increasing the size of the offering (a "Rule 462(b) Registration Statement"), filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Act"), which became effective upon filing, no other document with respect to the Initial Registration Statement has been filed with the Commission; and no stop order suspending the effectiveness of the Initial Registration Statement, any post-effective amendment thereto or the Rule 462(b) Registration Statement, if any, has been issued and no proceeding for that purpose has been initiated or, to the Company's knowledge, threatened by the Commission (any preliminary prospectus included in the Initial Registration Statement or filed with the Commission pursuant to Rule 424(a) of the rules and regulations of the Commission under the Act is hereinafter called a "Preliminary Prospectus"; the various parts of the Initial Registration Statement and the Rule 462(b) Registration Statement, if any, including all exhibits thereto and including the information contained in the form of final prospectus filed with the Commission pursuant to Rule 424(b) under the Act in accordance with Section 5(a) hereof and deemed by virtue of Rule 430A under the Act to be part of the Initial Registration Statement at the time it was declared effective, each as amended at the time such part of the Initial Registration Statement became effective or such part of the Rule 462(b) Registration Statement, if any, became or hereafter becomes effective, are hereinafter collectively called the "Registration Statement"; the Preliminary Prospectus relating to the Offered Securities that was included in the Registration Statement immediately prior to the Applicable Time (as defined in Section 1(c) hereof) is hereinafter called the "Pricing Prospectus"; such final prospectus, in the form first filed pursuant to Rule 424(b) under the Act, is hereinafter called the "Prospectus"; any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Act is hereinafter called a "Section 5(d)

Communication"; any Section 5(d) Communication that is a written communication within the meaning of Rule 405 under the Act is hereinafter called a "Section 5(d) Writing"; any "issuer free writing prospectus" as defined in Rule 433 under the Act relating to the Offered Securities is hereinafter called an "Issuer Free Writing Prospectus"); and any "bona fide electronic road show" as defined in Rule 433(h)(5) under the Act that has been made available without restriction to any person is hereinafter called a "broadly available road show";

(b) (A) No order preventing or suspending the use of any Preliminary Prospectus or any Issuer Free Writing Prospectus has been issued by the Commission, and (B) each Preliminary Prospectus, at the time of filing thereof, conformed in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder, and did not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; *provided, however*, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with the Underwriter Information (as defined in Section 9(b) of this Agreement);

(c) For the purposes of this Agreement, the "Applicable Time" is [·] p.m. (Eastern time) on the date of this Agreement. The Pricing Prospectus, as supplemented by the information listed on Schedule II(c) hereto, taken together (collectively, the "Pricing Disclosure Package"), as of the Applicable Time, did not, and as of each Time of Delivery (as defined in Section 4(a) of this Agreement) will not, include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; and each Issuer Free Writing Prospectus and each Section 5(d) Writing does not conflict with the information contained in the Registration Statement, the Pricing Prospectus or the Prospectus and each Issuer Free Writing Prospectus, each broadly available road show and each Section 5(d) Writing, as supplemented by and taken together with the Pricing Disclosure Package, as of the Applicable Time, did not, and as of each Time of Delivery will not, include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to statements or omissions made in reliance upon and in conformity with the Underwriter Information;

(d) The Registration Statement, at the time it was declared effective, conformed and the Prospectus and any further amendments or supplements to the Registration Statement and the Prospectus on the date when such prospectus, amendment, or supplement is filed will conform, in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder and do not and will not, as of the applicable effective date as to each part of the Registration Statement, as of the applicable filing date as to the Prospectus and any amendment or supplement thereto, and as of each Time of

Delivery, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; provided, however, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with the Underwriter Information;

(e) A registration statement on Form F-6 (File No. 333-[·]) in respect of the ADSs has been filed with the Commission; such registration statement in the form previously delivered to you and, excluding exhibits, to you for each of the other Underwriters, has been declared effective by the Commission in such form; no other document with respect to such registration statement has been filed with the Commission; no stop order suspending the effectiveness of such registration statement has been issued and no proceeding for that purpose has been initiated or threatened by the Commission (the various parts of such registration statement, including all exhibits thereto, each as amended at the time such part of the registration statement became effective, being hereinafter called the "ADS Registration Statement"); and the ADS Registration Statement when it became effective conformed, and any further amendments thereto will confirm, in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder, and did not, as of the applicable effective date, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; provided, however, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with the Underwriter Information;

(f) Neither the Company nor any of its subsidiaries has, since the date of the latest audited financial statements included in the Pricing Prospectus and the Prospectus, (i) sustained any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree or (ii) entered into any transaction or agreement (whether or not in the ordinary course of business) that is material to the Company and its subsidiaries taken as a whole or incurred any liability or obligation, direct or contingent, that is material to the Company and its subsidiaries taken as a whole, in each case, in each case otherwise than as set forth or contemplated in the Pricing Prospectus and the Prospectus; and, since the respective dates as of which information is given in the Registration Statement, the Pricing Prospectus and the Prospectus, there has not been (x) any change in the share capital (other than as a result of (i) the exercise, if any, of options or the award, if any, of options or restricted shares in the ordinary course of business pursuant to the Company's equity plans that are described in the Pricing Prospectus and the Prospectus or (ii) the issuance, if any, of shares upon conversion of Company securities as described in the Pricing Prospectus and the Prospectus) or long-term debt of the Company or any of its subsidiaries or (y) any material adverse change or effect, or any development involving a prospective material adverse change or effect, in or affecting (i) the business, properties, general affairs, management, financial position, shareholders' equity, prospects or

results of operations of the Company and its subsidiaries taken as a whole, or (ii) the ability of the Company to perform its obligations under this Agreement, including the issuance and sale of the ADSs, or to consummate the transactions contemplated in the Pricing Prospectus and the Prospectus (a "Material Adverse Effect");

(g) The Company and its subsidiaries have good and marketable title in fee simple to all real property that they are purported to own, if any, and good and marketable title to all personal property owned by them, in each case free and clear of all liens, encumbrances and defects except such as are described in the Pricing Prospectus and the Prospectus or such as do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and its subsidiaries; and any real property and buildings held under lease by the Company and its subsidiaries are held by them under valid, subsisting and enforceable leases with such exceptions as are not material and do not materially interfere with the use made and proposed to be made of such property and buildings by the Company and its subsidiaries;

(h) The Company and each of its subsidiaries has been (i) duly organized and is validly existing and in good standing under the laws of its jurisdiction of organization, with power and authority (corporate and other) to own its properties and conduct its business as described in the Pricing Prospectus and the Prospectus, and (ii) duly qualified as a foreign corporation for the transaction of business and is in good standing (where such concept exists) under the laws of each other jurisdiction in which it owns or leases properties or conducts any business so as to require such qualification, except, in the case of this clause (ii), where the failure to be so qualified or in good standing would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, and each subsidiary of the Company has been listed in the Registration Statement;

(i) The Company has an authorized share capital as set forth in the Pricing Prospectus and the Prospectus and all of the issued share capital of the Company has been duly and validly authorized and issued and is fully paid and non-assessable and conforms to the description of the Ordinary Shares contained in the Pricing Disclosure Package and Prospectus; and all of the issued share capital of each subsidiary of the Company has been duly and validly authorized and issued, is fully paid and non-assessable and (except, in the case of any foreign subsidiary, for directors' qualifying shares) is owned directly or indirectly by the Company, free and clear of all liens, encumbrances, equities or claims, except for such liens or encumbrances described in the Pricing Prospectus and the Prospectus;

(j) The Shares to be issued underlying the ADSs have been duly and validly authorized and, when issued and delivered against payment therefor as provided herein, will be duly and validly issued and fully paid and non-assessable and will conform to the description of the Ordinary Shares contained in the Pricing Disclosure Package and the Prospectus; and the issuance of the Shares is not

subject to any preemptive or similar rights; the Shares may be freely deposited by the Company with the Depositary against issuance of ADRs evidencing ADSs; the ADSs, when issued and delivered against payment therefor, will be freely transferable by the Company to or for the account of the several Underwriters and the initial purchasers thereof; and there are no restrictions on subsequent transfers of the Offered Securities, except as described in the Pricing Prospectus;

(k) The issue and sale of the ADSs to be sold by the Company hereunder, the deposit of the Shares being deposited with the Depositary against issuance of the ADRs evidencing the ADSs and the compliance by the Company with this Agreement and the Deposit Agreement, and the consummation of the transactions contemplated in this Agreement and the Pricing Prospectus and the Prospectus will not conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, (A) any indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any of the property or assets of the Company or any of its subsidiaries is subject, except, in the case of this clause (A) for such defaults, breaches, or violations that would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, (B) the memorandum and articles of association (or other applicable organizational document) of the Company or any of its subsidiaries, or (C) any statute or any judgment, order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of its subsidiaries or any of their properties; and no consent, approval, authorization, order, registration or qualification of or with any such court or governmental agency or body is required for the issue and sale of the ADSs, or the deposit of the Shares being deposited with the Depositary against issuance of ADRs evidencing the ADSs to be delivered or the consummation by the Company of the transactions contemplated by this Agreement, except such as have been obtained under the Act, the approval by the Financial Industry Regulatory Authority ("FINRA") of the underwriting terms and arrangements and such consents, approvals, authorizations, registrations or qualifications as may be required under state securities or Blue Sky laws in connection with the purchase and distribution of the ADSs by the Underwriters;

(l) Neither the Company nor any of its subsidiaries is (i) in violation of its memorandum and articles of association (or other applicable organizational document), (ii) in violation of any statute or any judgment, order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of its subsidiaries or any of their properties, or (iii) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which it is a party or by which it or any of its properties may be bound, except, in the case of the foregoing clauses (ii) and (iii), for such defaults as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect;

(m) The statements set forth in the Pricing Prospectus and Prospectus under the captions “Description of Share Capital and Articles of Association,” “Description of American Depositary Shares” and “Shares and American Depositary Shares Eligible for Future Sale”, insofar as they purport to constitute a summary of the terms of the Ordinary Shares and ADSs, insofar as they purport to describe the provisions of the laws and documents referred to therein, are accurate, complete and fair in all material respects;

(n) Other than as set forth in the Pricing Prospectus and the Prospectus, there are no legal or governmental proceedings pending to which the Company or any of its subsidiaries or, to the Company’s knowledge, any officer or director of the Company, is a party or of which any property of the Company or any of its subsidiaries or, to the Company’s knowledge, any officer or director of the Company, is the subject which, if determined adversely to the Company or any of its subsidiaries (or such officer or director), would individually or in the aggregate have a Material Adverse Effect; and, to the Company’s knowledge, no such proceedings are threatened or contemplated by governmental authorities or others;

(o) The Company is not and, after giving effect to the offering and sale of the ADSs and the application of the proceeds thereof as described in the Pricing Prospectus and the Prospectus, will not be an “investment company”, as such term is defined in the Investment Company Act of 1940, as amended (the “Investment Company Act”);

(p) At the time of filing the Initial Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company or any offering participant made a bona fide offer (within the meaning of Rule 164(h)(2) under the Act) of the ADSs, and at the date hereof, the Company was not and is not an “ineligible issuer,” as defined under Rule 405 under the Act;

(q) PricewaterhouseCoopers LLP, who have audited and certified certain financial statements of the Company and its subsidiaries, are independent public accountants as required by the Act and the rules and regulations of the Commission thereunder;

(r) The Company maintains a system of internal control over financial reporting (as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”)) that (i) complies with the requirements of the Exchange Act, (ii) has been designed by the Company’s principal executive officer and principal financial officer, or under their supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and (iii) is sufficient to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the Pricing Prospectus and the Prospectus, the Company’s

internal control over financial reporting is effective and the Company is not aware of any material weaknesses in its internal control over financial reporting;

(s) Since the date of the latest audited financial statements included in the Pricing Prospectus and the Prospectus, there has been no change in the Company's internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting;

(t) The Company maintains disclosure controls and procedures (as such term is defined in Rule 13a-15(e) under the Exchange Act) that comply with the requirements of the Exchange Act; such disclosure controls and procedures have been designed to ensure that material information relating to the Company and its subsidiaries is made known to the Company's principal executive officer and principal financial officer by others within those entities; and such disclosure controls and procedures are effective;

(u) This Agreement has been duly authorized, executed and delivered by the Company;

(v) The Deposit Agreement has been duly authorized and, when executed and delivered by the Company; and, assuming due authorization, execution and delivery by the Depositary, will constitute a valid and legally binding agreement of the Company, enforceable in accordance with its terms, subject, as to enforceability, bankruptcy, insolvency, reorganization and similar laws of general applicability relating to or affecting creditors' rights and to general equity principles, and upon the deposit of Shares in respect of the ADSs in accordance with the provisions of the Deposit Agreement, the ADSs, when issued, will be validly issued and fully paid, and upon issuance by the Depositary of the ADSs and ADRs evidencing the ADSs, such ADRs will be duly and validly issued and the persons in whose names the ADRs are registered will be entitled to the rights specified therein and in the Deposit Agreement; and the Deposit Agreement, the ADSs and the ADRs conform in all material respects to the descriptions thereof contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus;

(w) None of the Company or any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person associated with or acting on behalf of the Company or any of its subsidiaries has (i) directly or indirectly made, offered, promised or authorized any unlawful payment, contribution, gift, entertainment or other unlawful benefit or expense or taken any act in furtherance thereof; (ii) made, offered, promised or authorized any direct or indirect unlawful payment; or (iii) violated or is in violation of any provision of the U.S. Foreign Corrupt Practices Act of 1977, as amended, the Bribery Act 2010 of the United Kingdom or any other applicable anti-bribery or anti-corruption law;

(x) The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with the requirements of applicable anti-

money laundering laws, including, but not limited to, the Bank Secrecy Act of 1970, as amended by the USA PATRIOT ACT of 2001, and the rules and regulations promulgated thereunder, and the anti-money laundering laws of the various jurisdictions in which the Company and its subsidiaries conduct business (collectively, the "Money Laundering Laws") and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened;

(y) None of the Company or any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company or any of its subsidiaries is currently the subject or the target of any sanctions administered or enforced by either the U.K. or U.S. government, including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury ("OFAC"), or the U.S. Department of State and including, without limitation, the designation as a "specially designated national" or "blocked person," the European Union, Her Majesty's Treasury, the United Nations Security Council, or other relevant sanctions authority (collectively, "Sanctions"), nor is the Company or any of its subsidiaries located, organized, or resident in a country or territory that is the subject or target of Sanctions, and the Company will not directly or indirectly use the proceeds of the offering of the ADSs hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person, or in any country or territory, that, at the time of such funding, is the subject or the target of Sanctions or (ii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions. No provision of this Section 1(y) shall apply to any person if and to the extent that it violates any provision of Council Regulation (EC) No 2271/1996 of November 22 1996 (or any law or regulation implementing such regulation in any member state of the European Union or the United Kingdom), or any similar blocking or anti-boycott law, regulation or statute in force from time to time, and, in such case, the legality, validity and enforceability of this Section 1(y) shall not otherwise be affected;

(z) The consolidated financial statements included in the Registration Statement, the Pricing Prospectus and the Prospectus, together with the related schedules and notes, present fairly in all material respects the financial position of the Company and its subsidiaries at the dates indicated and the statement of operations, stockholders' equity and cash flows of the Company and its subsidiaries for the periods specified; said financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("GAAP") applied on a consistent basis throughout the periods involved. The supporting schedules, if any, present fairly all material respects in accordance with GAAP the information required to be stated therein. The selected consolidated financial data and the summary consolidated financial information included in the Registration Statement, the Pricing Prospectus and the Prospectus present fairly in all material respects the information shown therein and have been compiled on a basis consistent with that

of the audited financial statements included therein. Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included in the Registration Statement, the Pricing Prospectus or the Prospectus under the Act or the rules and regulations promulgated thereunder.

(aa) From the time of initial confidential submission of a registration statement relating to the Offered Securities with the Commission (or, if earlier, the first date on which a Section 5(d) Communication was made) through the date hereof, the Company has been and is an "emerging growth company" as defined in Section 2(a)(19) of the Act (an "Emerging Growth Company");

(bb) There are no persons with registration rights or other similar rights to have any securities registered pursuant to the Registration Statement or otherwise registered by the Company under the Act except as have been validly waived or complied with in connection with the offering of the ADSs;

(cc) No labor disturbance by or dispute with current or former employees or officers of the Company or any of its subsidiaries exists or, to the Company's knowledge, is contemplated or threatened, and the Company is not aware of any existing or imminent labor disturbance by, or dispute with, the employees of any of the Company's or any of its subsidiaries' principal suppliers, manufacturers or contractors. Neither the Company nor any of its subsidiaries is a party to any collective bargaining agreement.

(dd) The Company and its subsidiaries have insurance covering their respective properties, operations, personnel and businesses, including business interruption insurance, which insurance is in amounts and insures against such losses and risks, that in the Company's reasonable judgement, are reasonable and is ordinary and customary for comparable companies in the same or similar businesses; and neither the Company nor any of its subsidiaries has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage at reasonable cost from similar insurers as may be necessary to continue its business;

(ee) The Company's board of directors meets the independence requirements of, and has established an audit committee, a compensation committee and a nominating and corporate governance committee, in each case, that meets the independence requirements of, the rules and regulations of the Commission and the NASDAQ Global Market ("NASDAQ");

(ff) The Company and its subsidiaries and its and their respective directors, officers and employees, and to the Company's knowledge, its and their respective agents, affiliates and representatives, are, and at all times have been, in compliance with all Health Care Laws (defined herein), including, but not limited to, the rules and regulations of the Food and Drug Administration ("FDA"), the U.S. Department of Health and Human Services Office of Inspector General, the Centers for Medicare & Medicaid Services, the Office for Civil Rights, the Department of

Justice and any other governmental agency or body having jurisdiction over the Company or any of its properties, and has not engaged in any activities which are, as applicable, cause for false claims liability, civil penalties, or mandatory or permissive exclusion from Medicare, Medicaid, or any other local, state or federal healthcare program, other than for such instances of non-compliance which would not reasonably be expected to result in a Material Adverse Effect. For purposes of this Agreement, "Health Care Laws" shall mean the federal Anti-kickback Statute (42 U.S.C. § 1320a-7b(b)), the Physician Payments Sunshine Act (42 U.S.C. § 1320a-7h), the civil False Claims Act (31 U.S.C. §§ 3729 et seq.), the criminal False Claims Act (42 U.S.C. § 1320a-7b(a)), all criminal laws relating to health care fraud and abuse, including but not limited to 18 U.S.C. Sections 286, 287, 1347 and 1349, and the health care fraud criminal provisions under the Health Insurance Portability and Accountability Act of 1996 (42 U.S.C. §§ 1320d et seq.) ("HIPAA"), the exclusion laws (42 U.S.C. § 1320a-7), the civil monetary penalties law (42 U.S.C. § 1320a-7a), HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (42 U.S.C. §§ 17921 et seq.), the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §§ 301 et seq.), Medicare (Title XVIII of the Social Security Act), Medicaid (Title XIX of the Social Security Act), Medicaid Drug Rebate Program (42 U.S.C. § 1396r-8), Medicare average sales price reporting (42 U.S.C. § 1395w-3a), the Public Health Service Act (42 U.S.C. § 256b), the VA Federal Supply Schedule (38 U.S.C § 8126) or the rules and regulations of any other federal, state or local governmental or regulatory body or authority. Neither the Company nor any of its subsidiaries is a party to or has any ongoing reporting obligations pursuant to any corporate integrity agreement, deferred prosecution agreement, monitoring agreement, consent decree, settlement order, plan of correction or similar agreement imposed by any governmental authority. Neither the Company nor any of its subsidiaries has received any notification, correspondence or any other written communication, including, without limitation, any FDA Form 483, notice of adverse finding, warning letter, untitled letter or other correspondence or notice from the FDA or any similar regulatory authority, or any notification of any pending or threatened claim, suit, proceeding, hearing, enforcement, investigation, arbitration or other action, from any governmental authority of non-compliance by, or liability of, the Company or its subsidiaries under any Health Care Laws;

(gg) Each of the Company and its subsidiaries possesses, and is in compliance with the terms of, all applications, certificates, approvals, clearances, registrations, exemptions, franchises, licenses, permits, consents and other authorizations necessary to conduct their respective businesses (collectively, "Licenses"), issued by the appropriate Governmental Authorities, including, without limitation, all Licenses required by the FDA, or any component thereof, the National Institutes of Health ("NIH") and/or by any other U.S., state, local or foreign government or drug regulatory agency (collectively, the "Regulatory Agencies"), other than for such instances of non-compliance which would not reasonably be expected to result in a Material Adverse Effect. All Licenses are in full force and effect and neither the Company nor any of its subsidiaries is in violation of any term or conditions of any License other than for such violations which would not reasonably be expected to result in a Material Adverse Effect. Each of the

Company and its subsidiaries has materially fulfilled and performed all of its respective obligations with respect to the Licenses and, to the Company's knowledge, no event has occurred which allows, or after notice or lapse of time would allow, revocation or termination thereof or results in any other impairment of the rights of the holder of any License. Neither the Company nor any of its subsidiaries has received any written notice of proceedings relating to the revocation or modification of any Licenses and no Regulatory Agency has taken any action to limit, suspend or revoke any License possessed by the Company;

(hh) The pre-clinical studies and clinical trials that are described in the Registration Statement, the Pricing Prospectus and the Prospectus were and, if still pending, are being, conducted in all material respects in accordance with the protocols submitted to the FDA or any foreign governmental body exercising comparable authority, procedures and controls pursuant to, where applicable, accepted professional and scientific standards, and all applicable laws and regulations; the descriptions of the pre-clinical studies and clinical trials conducted by or, to the Company's knowledge, on behalf of the Company, and the results thereof, contained in the Registration Statement, the Pricing Prospectus and the Prospectus are accurate and complete in all material respects; the Company is not aware of any other pre-clinical studies or clinical trials, the results of which reasonably call into question the results described in the Registration Statement, the Pricing Prospectus and the Prospectus; and the Company has not received any notices or correspondence from the FDA, any foreign, state or local governmental body exercising comparable authority or any Institutional Review Board requiring the termination, suspension, material modification or clinical hold of any pre-clinical studies or clinical trials conducted by or on behalf of the Company:

(ii) Neither the Company nor its subsidiaries, nor any of its or their respective officers, employees or directors, nor any of its or their respective agents or clinical investigators, has been excluded, suspended or debarred from participation in any U.S. federal health care program or human clinical research or, to the Company's knowledge, is subject to a governmental inquiry, investigation, proceeding, or other similar action that would reasonably be expected to result in debarment, suspension, or exclusion, or convicted of any crime or engaged in any conduct that would reasonably be expected to result in debarment under 21 U.S.C. § 335a;

(jj) Except in each case (a) as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect, and (b) as otherwise disclosed in the Pricing Prospectus and the Prospectus, the Company owns or has valid, binding and enforceable licenses or other rights to practice and use all patents and patent applications, copyrights, trademarks, trademark registrations, service marks, service mark registrations, trade names, service names and know-how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures) and all other technology and intellectual property rights necessary for, or used in the conduct, or the proposed conduct, of the business of the Company in the manner described in the Pricing

Prospectus and the Prospectus (collectively, the "Company Intellectual Property"), and, to the Company's knowledge, the conduct of its and its subsidiaries' respective business (including the development and commercialization of the product candidates described in the Pricing Prospectus and the Prospectus) has not and will not infringe or misappropriate any intellectual property rights of others; other than as disclosed in the Pricing Prospectus and the Prospectus, to the knowledge of the Company there are no rights of third parties (except for Cancer Research Technology Limited ("CRT") in a patent family owned jointly by the Company and CRT) to any of the intellectual property owned by the Company, and such intellectual property is owned by the Company free and clear of all material liens, security interests, or encumbrances; other than as disclosed in the Pricing Prospectus and the Prospectus, to the knowledge of the Company, the patents, trademarks and copyrights owned or licensed by the Company that are included within the Company Intellectual Property are valid, enforceable and subsisting; to the Company's knowledge, there is no infringement by third parties of any of the Company Intellectual Property; other than as disclosed in the Pricing Prospectus and the Prospectus, (i) neither the Company nor its subsidiaries, to the knowledge of the Company, is obligated to pay a material royalty, grant a license, or provide other material consideration to any third party in connection with the Company Intellectual Property, (ii) no action, suit, claim or other proceeding is pending or, to the knowledge of the Company, is threatened, alleging that the Company or its subsidiaries is infringing, misappropriating, diluting or otherwise violating any rights of others with respect to any of the Company's product candidates, processes or intellectual property, and the Company is unaware of any facts which could form a reasonable basis for any such action, suit, proceeding or claim, (iii) no action, suit, claim or other proceeding is pending or, to the knowledge of the Company, is threatened, challenging the validity, enforceability, scope, registration, ownership or use of any of the Company's Intellectual Property, (iv) no action, suit, claim or other proceeding is pending or, to the knowledge of the Company, is threatened, challenging the Company's rights in or to any Company Intellectual Property, (v) the Company has not received written notice of any claim of infringement, misappropriation or conflict with any asserted rights of others with respect to any of the Company's products, proposed products, processes or Company Intellectual Property, (vi) to the knowledge of the Company, the development, manufacture, sale, and any currently proposed use of any of the products, proposed products or processes of the Company referred to in the Pricing Prospectus and the Prospectus, in the current or proposed conduct of the business of the Company, do not currently, and will not upon commercialization, to the knowledge of the Company, infringe any valid patent claim or other valid intellectual property right of any third party, (vii) to the knowledge of the Company, no third party (except for CRT in a patent family owned jointly by the Company and CRT) has any ownership right in or to any Company Intellectual Property in any field of use that is exclusively licensed to the Company, other than any licensor to the Company of such Company Intellectual Property, (viii) to the knowledge of the Company, no employee, consultant or independent contractor of the Company or any of its subsidiaries is in or has ever been in violation in any material respect of any term of any employment

contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement nondisclosure agreement or any restrictive covenant to or with a former employer or independent contractor where the basis of such violation relates to such employee's employment or independent contractor's engagement with the Company or actions undertaken while employed or engaged with the Company, (ix) the Company has taken reasonable measures to protect its confidential information and trade secrets and to maintain and safeguard the Company's Intellectual Property, including the execution of appropriate nondisclosure and confidentiality agreements, and to the Company's knowledge, no employee of the Company is in or has been in violation of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement, or any restrictive covenant to or with a former employer where the basis of such violation relates to such employee's employment with the Company, (x) the Company has taken reasonable measures to comply with the terms of each agreement pursuant to which the Company's Intellectual Property has been licensed to the Company, and, to the Company's knowledge, all such agreements are in full force and effect,

(kk) All patents and patent applications owned by or licensed to the Company or under which the Company has rights have, to the knowledge of the Company, been duly and properly filed and maintained; to the knowledge of the Company, there are no material defects in any of the patents or patent applications disclosed in the Registration Statement and the Prospectus as being owned by the Company and its Subsidiaries; to the knowledge of the Company, the parties prosecuting such applications have complied with their duty of candor and disclosure to the USPTO in connection with such applications; and the Company is not aware of any facts required to be disclosed to the USPTO that were not disclosed to the USPTO and which would preclude the grant of a patent in connection with any such application or could form the basis of a finding of invalidity with respect to any patents that have issued with respect to such applications;

(ll) Any statistical, industry-related and market-related data included in the Pricing Prospectus and the Prospectus are based on or derived from sources that the Company believes, after reasonable inquiry, to be reliable and accurate and, to the extent required, the Company has obtained the written consent to the use of such data from such sources, if required;

(mm) The Company and its subsidiaries possess all licenses, certificates, permits and other authorizations issued by, and have made all declarations and filings with, the appropriate federal, state, local or foreign governmental or regulatory authorities having jurisdiction over the Company and its subsidiaries that are necessary for the ownership or lease of their respective properties or the conduct of their respective businesses as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, except where the failure to possess or make the same would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; and except as described in the

Registration Statement, the Pricing Disclosure Package and the Prospectus, neither the Company nor any of its subsidiaries has received written notice of any revocation or modification of any such license, certificate, permit or authorization, except where such revocation or modification would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect;

(nn) The Company and each of its subsidiaries (i) has duly and timely filed all necessary U.K., U.S. and non-U.S. (federal, state, local and foreign) tax returns (or properly requested extensions with respect to such returns), and such returns were when filed, and remain, complete and correct (ii) has paid all U.K., non-U.S. and U.S. federal, state and local taxes required to be paid and any related assessments, fines, penalties or governmental charges due and payable for which it is liable, except as are being contested in good faith by appropriate proceedings, and (iii) does not have any tax deficiency or claims outstanding or assessed or, to its knowledge, proposed against it, except, in each of (i), (ii) and (iii) above, as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. The accruals and reserves on the books and records of the Company and its subsidiaries in respect of tax liabilities for any taxable period not yet finally determined are adequate to meet any assessments and related liabilities for any such period;

(oo) Except as described in the Pricing Prospectus and the Prospectus, all dividends and other distributions declared and payable on the Shares may under the current laws and regulations of the United Kingdom may be paid to U.S. shareholders in U.S. dollars;

(pp) Except as described in the "Material Income Tax Considerations—U.K. Taxation" section of the Pricing Prospectus and the Prospectus, and subject to the description therein, there are no transfer taxes, stamp duty, stamp duty reserve tax or other similar fees or charges ("Transfer Taxes"), payable by or on behalf of the Underwriters in connection with (i) the issuance and delivery of the Shares by the Company to the Depositary for the purposes of the initial public offer in the manner prescribed by the Deposit Agreement, (ii) the issuance and delivery of the ADSs (or the ADRs evidencing the ADSs) by the Depositary to or for the account of the Underwriters for the purposes of the initial public offering in the manner contemplated by this Agreement and the Deposit Agreement, (iii) the sale and delivery by the Underwriters of the ADSs to the initial purchasers thereof, and (iv) the execution and delivery of this Agreement;

(qq) The Company and each of its subsidiaries is and has at all times been resident and centrally managed and controlled for tax purposes solely in its jurisdiction of incorporation;

(rr) The choice of the law of the State of New York as the governing law of this Agreement is a valid choice of law under English law and will be honored by English courts. The Company has the power to submit, and pursuant to Section 18 of this Agreement and Section [·] of the Deposit Agreement, has legally, validly,

effectively and irrevocably submitted, to the personal jurisdiction of (i) the federal courts of the United States located in the City and County of New York, Borough of Manhattan or (ii) the courts of the State of New York located in the City and County of New York, Borough of Manhattan (collectively, the "Specified Courts"), and the Company has legally, validly, effectively and irrevocably designated, appointed and authorized an agent for service of process in any action arising out of or relating to this Agreement or the Offered Securities in any Specified Court. The Company is not entitled to any immunity under English law from any legal proceedings to enforce this Agreement in respect of itself or its property. To the extent that the Company or any of its respective properties, assets or revenues may have been or may hereafter become entitled to any such right of immunity in any court in which proceedings may at any time be commenced, with respect to the Company's obligations, liabilities or any other matter under or arising out of or in connection with this Agreement, the Company waives or will waive such right to the extent permitted by law and has consented to such relief and enforcement as provided in Section 18 of this Agreement and Section [·] of the Deposit Agreement. The indemnification and contribution provisions set forth in Section 9 hereof do not contravene English law;

(ss) Except as described in the "Share Capital Reorganization and Reregistration" section of the Pricing Prospectus, no liability to tax will arise to the Company or any of its subsidiaries as a result of or in connection with the share capital reorganization described therein as would reasonably be expected to have a Material Adverse Effect.

(tt) The Company has not taken and will not take, directly or indirectly, any action that is designed to or that has constituted or might reasonably be expected to cause or result in stabilization or manipulation of the price of the ADSs;

(uu) Neither the Company nor any of its subsidiaries is a party to any contract, agreement or understanding with any person (other than this Agreement) that would give rise to a valid claim against the Company or any of its subsidiaries or any Underwriter for a brokerage commission, finder's fee or like payment in connection with the offering and sale of the ADSs;

(vv) No relationship, direct or indirect, exists between or among the Company or any of its subsidiaries, on the one hand, and the directors, officers, shareholders, customers or suppliers of the Company or any of its subsidiaries, on the other, that is required by the Act to be described in the Registration Statement and the Prospectus and that is not so described in such documents and in the Registration Statement, the Pricing Disclosure Package and the Prospectus;

(ww) There are no contracts, arrangements or documents which are required to be described in the Registration Statement or to be filed as exhibits thereto which have not been so described and filed as required;

(xx) Except as disclosed in the Registration Statement and the Prospectus, (a) there has been no security breach or other material compromise of any of the Company's information technology and computer systems, networks, hardware, software, sensitive data (including the sensitive or proprietary data of its customers, employees, suppliers, and vendors maintained by or on behalf of the Company), equipment or technology (collectively, "IT Systems and Data") and (b) the Company has not been notified of, and has no knowledge of any event or condition that would reasonably be expected to result in, any security breach or other material compromise to its IT Systems and Data;

(yy) Neither the Company, nor any of their respective officers, directors and employees, nor any of their respective agents, contractors or licensees (if any), nor any of their respective business operations, is in violation of any applicable privacy or cybersecurity laws. The Company has complied and is presently in compliance with all internal policies and contractual obligations relating to (a) the privacy and security of IT Systems and Data and (b) the implementation of commercially reasonable measures to protect such IT Systems and Data from unauthorized use, access, misappropriation or modification, except as would not, in the case of this clause, individually or in the aggregate, have a Material Adverse Effect. The Company has implemented backup and disaster recovery technology consistent with industry standards and practices. The Company has also operated its business in a manner compliant with all other privacy, data security and data protection laws, regulations, and industry standards applicable to the Company's collection, use, transfer, protection, disposal, disclosure, handling, storage and analysis of its personal data; and

(zz) The Company has implemented an information security program that (a) identifies internal and external risks to the security of the IT Systems and Data, including any personally identifiable information; (b) implements, monitors and improves adequate and effective administrative, electronic and physical safeguards to control those risks and safeguard the security, confidentiality, integrity and availability of IT Systems and Data; (c) protects against unauthorized access to Company systems and IT Systems and Data (including on the systems of third parties with access to such Company systems or IT Systems and Data); (d) maintains notification procedures in the case of any breach of security compromising data containing personally identifiable information; and (e) prohibits any unauthorized access of any non-Company systems.

2. Subject to the terms and conditions herein set forth, (a) the Company agrees to issue and sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at a purchase price per ADS of $[·], the number of Firm ADSs set forth opposite the name of such Underwriter in Schedule I hereto and (b) in the event and to the extent that the Underwriters shall exercise the election to purchase Optional ADSs as provided below, the Company agrees to issue and sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at the purchase price per ADS set forth in clause (a)

of this Section 2 (provided that the purchase price per Optional ADS shall be reduced by an amount per ADS equal to any dividends or distributions declared by the Company and payable on the Firm ADSs but not payable on the Optional ADSs), that portion of the number of Optional ADSs as to which such election shall have been exercised (to be adjusted by you so as to eliminate fractional ADSs) determined by multiplying such number of Optional ADSs by a fraction, the numerator of which is the maximum number of Optional ADSs which such Underwriter is entitled to purchase as set forth opposite the name of such Underwriter in Schedule I hereto and the denominator of which is the maximum number of Optional ADSs that all of the Underwriters are entitled to purchase hereunder.

(i) The Company hereby grants to the Underwriters the right to purchase at their election up to [·] Optional ADSs, at the purchase price per ADS set forth in the paragraph above, for the sole purpose of covering sales of ADSs in excess of the number of Firm ADSs, provided that the purchase price per Optional ADS shall be reduced by an amount per ADS equal to any dividends or distributions declared by the Company and payable on the Firm ADSs but not payable on the Optional ADSs. Any such election to purchase Optional ADSs may be exercised only by written notice from the Representatives to the Company, given within a period of 30 calendar days after the date of this Agreement, setting forth the aggregate number of Optional ADSs to be purchased and the date on which such Optional ADSs are to be delivered, as determined by the Representatives but in no event earlier than the First Time of Delivery (as defined in Section 4 hereof) or, unless the Representatives and the Company otherwise agree in writing, earlier than two or later than ten business days after the date of such notice.

3. Upon the authorization by you of the release of the Firm ADSs, the several Underwriters propose to offer the Firm ADSs for sale upon the terms and conditions set forth in the Pricing Prospectus and the Prospectus.

4. (a) The ADSs to be purchased by each Underwriter hereunder, in definitive or book-entry form, and in such authorized denominations and registered in such names as the Representatives may request upon at least forty-eight hours' prior notice to the Company shall be delivered by or on behalf of the Company to the Representatives, by means of the creation of an appropriate book-entry interest for benefit of the Underwriters through the facilities of the Depository Trust Company ("DTC"), for the account of such Underwriter, against payment by or on behalf of such Underwriter of the purchase price therefor by wire transfer of Federal (same-day) funds to the account specified by the Company to the Representatives at least forty-eight hours in advance. The Company will cause the certificates, if any, representing the Offered Securities, if any, to be made available for checking and packaging at least twenty-four hours prior to the Time of Delivery (as defined below) with respect thereto at the office of DTC or its designated custodian (the "Designated Office"). The time and date of such delivery and payment shall be, with respect to the Firm ADSs, 9:30 a.m., New

York City time, on [·], 2019 or such other time and date as the Representatives and the Company may agree upon in writing, and, with respect to the Optional ADSs, 9:30 a.m., New York time, on the date specified by the Representatives in the written notice given by the Representatives of the Underwriters' election to purchase such Optional ADSs, or such other time and date as the Representatives and the Company may agree upon in writing. Such time and date for delivery of the Firm ADSs is herein called the "First Time of Delivery", such time and date for delivery of the Optional ADSs, if not the First Time of Delivery, is herein called the "Second Time of Delivery", and each such time and date for delivery is herein called a "Time of Delivery".

(b) The documents to be delivered at each Time of Delivery by or on behalf of the parties hereto pursuant to Section 8 hereof, including the cross receipt for the ADSs and any additional documents requested by the Underwriters pursuant to Section 8(m) hereof, will be delivered at the offices of Cooley LLP, 55 Hudson Yards, New York, New York 10001 (the "Closing Location"), and the ADSs will be delivered at the Designated Office, all at such Time of Delivery. A meeting will be held at the Closing Location at [·] p.m., New York City time, on the New York Business Day next preceding such Time of Delivery, at which meeting the final drafts of the documents to be delivered pursuant to the preceding sentence will be available for review by the parties hereto. For the purposes of this Agreement, "New York Business Day" shall mean each Monday, Tuesday, Wednesday, Thursday and Friday which is not a day on which banking institutions in New York City are generally authorized or obligated by law or executive order to close.

5. The Company agrees with each of the Underwriters:

(a) To prepare the Prospectus in a form approved by you and to file such Prospectus pursuant to Rule 424(b) under the Act not later than the Commission's close of business on the second business day following the execution and delivery of this Agreement, or, if applicable, such earlier time as may be required by Rule 430A(a)(3) under the Act; to make no further amendment or any supplement to the Registration Statement or the Prospectus prior to the last Time of Delivery which shall be disapproved by you promptly after reasonable notice thereof; to advise you, promptly after it receives notice thereof, of the time when any amendment to the Registration Statement has been filed or becomes effective or any amendment or supplement to the Prospectus has been filed and to furnish you with copies thereof; to file promptly all material required to be filed by the Company with the Commission pursuant to Rule 433(d) under the Act; to advise you, promptly after it receives notice thereof, of the issuance by the Commission of any stop order or of any order preventing or suspending the use of any Preliminary Prospectus or other prospectus in respect of the Offered Securities, of the suspension of the qualification of the Offered Securities for offering or sale in any jurisdiction, of the initiation or threatening of any proceeding for any such purpose, or of any request by the Commission for the amending or supplementing of the Registration Statement or the Prospectus or for additional information; and, in the event of the issuance of any stop order or of any order preventing or suspending the use of any

Preliminary Prospectus or other prospectus or suspending any such qualification, to promptly use its best efforts to obtain the withdrawal of such order;

(b) Promptly from time to time to take such action as you may reasonably request to qualify the ADSs for offering and sale under the securities laws of such jurisdictions as you may request and to use reasonably commercial efforts to comply with such laws so as to permit the continuance of sales and dealings therein in such jurisdictions for as long as may be necessary to complete the distribution of the ADSs, provided that in connection therewith the Company shall not be required to qualify as a foreign corporation (where not otherwise required) or to file a general consent to service of process in any jurisdiction (where not otherwise required);

(c) Prior to 10:00 a.m., New York City time, on the New York Business Day next succeeding the date of this Agreement and from time to time, to furnish the Underwriters with written and electronic copies of the Prospectus in New York City in such quantities as you may reasonably request, and, if the delivery of a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is required at any time prior to the expiration of nine months after the time of issue of the Prospectus in connection with the offering or sale of the ADSs and if at such time any event shall have occurred as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made when such Prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is delivered, not misleading, or, if for any other reason it shall be necessary during such same period to amend or supplement the Prospectus in order to comply with the Act, to notify you and upon your request to prepare and furnish without charge to each Underwriter and to any dealer in securities as many written and electronic copies as you may from time to time reasonably request of an amended Prospectus or a supplement to the Prospectus which will correct such statement or omission or effect such compliance; and in case any Underwriter is required to deliver a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) in connection with sales of any of the ADSs at any time nine months or more after the time of issue of the Prospectus, upon your request but at the expense of such Underwriter, to prepare and deliver to such Underwriter as many written and electronic copies as you may request of an amended or supplemented Prospectus complying with Section 10(a)(3) of the Act;

(d) To make generally available to its securityholders as soon as practicable, (which may be satisfied by filing with the Commission's Electronic Data Gathering, Analysis and Retrieval System ("EDGAR")), but in any event not later than sixteen months after the effective date of the Registration Statement (as defined in Rule 158(c) under the Act), an earnings statement of the Company and its subsidiaries (which need not be audited) complying with Section 11(a) of the Act and the rules and regulations of the Commission thereunder (including, at the option of the Company, Rule 158);

(e) (i) During the period beginning from the date hereof and continuing to and including the date 180 days after the date of the Prospectus (the "Lock-Up Period"), not to (i) offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, or file with or confidentially submit to the Commission a registration statement under the Act relating to, any securities of the Company that are substantially similar to the Shares or ADSs, including but not limited to, Ordinary Shares, any options or warrants to purchase Ordinary Shares or any securities that are convertible into or exchangeable for, or that represent the right to receive, Ordinary Shares or any such substantially similar securities, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Ordinary Shares or any such other securities that are substantially similar to the Shares, whether any such transaction described in clauses (i) or (ii) above is to be settled by delivery of Ordinary Shares or such other securities, in cash or otherwise (other than the Shares to be sold hereunder or pursuant to employee option plans existing on, or upon the conversion or exchange of convertible or exchangeable securities outstanding as of, the date of this Agreement) or (iii) publicly disclose the intention to do any of the foregoing, in each case, without the prior written consent of the Representatives; provided, however, that the restrictions in the foregoing sentence shall not apply to (a) the ADSs to be sold hereunder; (b) Shares or any securities (including without limitation options, restricted stock or restricted stock units) convertible into, or exercisable for, Shares pursuant to any employee stock option plan, incentive plan, stock plan, dividend reinvestment plan or otherwise in equity compensation arrangements in place as of the Applicable Time and as described in the Pricing Disclosure Package; (c) the grant of awards pursuant to employee equity-based compensation plans, incentive plans, stock plans, or other arrangements in place as of the Applicable Time and described in the Pricing Disclosure Package; (d) the filing of a registration statement on Form S-8 in connection with the registration of Shares issuable under any employee equity based compensation plan, incentive plan, stock plan, dividend reinvestment plan adopted and approved by the Company's board of directors prior to the Applicable Time and as described in the Pricing Disclosure Package; and (e) the issuance of up to 5% of the outstanding Shares in connection with the acquisition of the assets of, or a majority or controlling portion of the equity of, or a joint venture with another entity in connection with its acquisition by the Company or any of its subsidiaries of such entity; provided that each recipient of any Shares issued or sold pursuant to clause (e) above executes and delivers to the Representatives prior to such issuance or sale (as the case may be) an agreement having substantially the same terms as the lock-up letters described in Section 8(j) of this agreement;

(ii) If the Representatives, in their sole discretion, agree to release or waive the restrictions set forth in a lock-up letter described in Section 8(l) hereof for an officer or director of the Company and provide the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, the Company agrees to announce the

impending release or waiver by a press release substantially in the form of Annex I hereto through a major news service at least two business days before the effective date of the release or waiver.

(f) During a period of three years from the effective date of the Registration Statement, so long as the Company is subject to the reporting requirements of either Section 13 or Section 15(d) of the Exchange Act, to furnish to its shareholders as soon as practicable after the end of each fiscal year an annual report (including a balance sheet and statements of income, shareholders' equity and cash flows of the Company and its consolidated subsidiaries certified by independent public accountants) and, as soon as practicable after the end of each of the first three quarters of each fiscal year (beginning with the fiscal quarter ending after the effective date of the Registration Statement), to make available to its shareholders consolidated summary financial information of the Company and its subsidiaries for such quarter in reasonable detail; provided that no reports, documents or other information need to be furnished pursuant to this Section 5(f) to the extent that they are available on the Commission's EDGAR system;

(g) During a period of three years from the effective date of the Registration Statement, so long as the Company is subject to the reporting requirements of either Section 13 or Section 15(d) of the Exchange Act, to furnish to you copies of all reports or other communications (financial or other) furnished to stockholders, and to deliver to you (i) as soon as they are available, copies of any reports and financial statements furnished to or filed with the Commission or any national securities exchange on which any class of securities of the Company is listed; and (ii) such additional information concerning the business and financial condition of the Company as you may from time to time reasonably request (such financial statements to be on a consolidated basis to the extent the accounts of the Company and its subsidiaries are consolidated in reports furnished to its stockholders generally or to the Commission); provided that no reports, documents or other information need to be furnished pursuant to this Section 5(f) to the extent that they are available on the Commission's EDGAR system;

(h) To use the net proceeds received by it from the sale of the ADSs pursuant to this Agreement in the manner specified in the Pricing Prospectus and the Prospectus under the caption "Use of Proceeds";

(i) Prior to each Time of Delivery to deposit Shares with the Depositary in accordance with the provisions of the Deposit Agreement and otherwise to comply with the Deposit Agreement so that ADSs and ADRs evidencing ADSs will be executed (and, if applicable, countersigned) and issued by the Depositary against receipt of such Shares and delivered to the Underwriters at such Time of Delivery;

(j) To use its best efforts to list for trading, subject to notice of issuance, the ADSs on NASDAQ;

(k) To file with the Commission such information on Form 10-Q or Form 10-K as may be required by Rule 463 under the Act;

(l) If the Company elects to rely upon Rule 462(b), the Company shall file a Rule 462(b) Registration Statement with the Commission in compliance with Rule 462(b) by 10:00 P.M., Washington, D.C. time, on the date of this Agreement, and the Company shall at the time of filing either pay to the Commission the filing fee for the Rule 462(b) Registration Statement or give irrevocable instructions for the payment of such fee pursuant to Rule 111(b) under the Act;

(m) Upon request of any Underwriter, to furnish, or cause to be furnished, to such Underwriter an electronic version of the Company's trademarks, servicemarks and corporate logo for use on the website, if any, operated by such Underwriter for the purpose of facilitating the on-line offering of the ADSs (the "License"); provided, however, that the License shall be used solely for the purpose described above, is granted without any fee and may not be assigned or transferred;

(n) To promptly notify you if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) completion of the distribution of the ADSs within the meaning of the Act and (ii) completion of the Lock-Up Period referred to in Section 5(e) hereof;

(o) To make all payments under this Agreement without withholding or deduction for or on account of any present or future taxes, levies, imposts, duties, fees, assessments or governmental charges whatsoever, imposed or levied by or on behalf of any taxing authority unless the Company is or becomes required by applicable law to deduct or withhold such taxes, levies, imposts, fees, duties, assessments or other governmental charges. In that event, the Company shall pay such additional amounts as may be necessary in order to ensure that the net amounts received by each Underwriter after such withholding or deduction shall equal the amounts that would have been received if no withholding or deduction had been made;

(p) If the performance by the Underwriters of any of their obligations under this Agreement shall represent for VAT purposes under any applicable law the making by the Underwriters of any supply of goods or services to the Company (to the extent applicable), the Company shall pay to the Underwriters, in addition to the amounts otherwise payable by the Company pursuant to this Agreement, an amount equal to the VAT chargeable on any such supply of goods and services provided that the Underwriters have issued the Company with an appropriate VAT invoice in respect of the supply to which the payment relates. Where a sum (a "Relevant Sum") is paid or reimbursed to the Underwriters pursuant to this Agreement in respect of any cost, expense or other amount and that cost, expense or other amount includes an amount in respect of irrecoverable VAT (the "VAT Element") which has been certified as such by the Underwriters (acting reasonably), then the Company, to the extent applicable, shall, in addition, pay an amount equal

to the VAT Element to the Underwriters. For the purposes of this Agreement, "VAT" means value added tax as provided for in the Value Added Tax Act 1994 ("VATA") and subordinate legislation made under VATA as amended, modified or re-enacted (whether before or after the date of this Agreement) and any similar sales, consumption, use or turnover tax whether within the United Kingdom or elsewhere in the world; and

(q) The Company will deliver to the Representatives, on the date of execution of this Agreement, properly completed and executed Certifications Regarding Beneficial Owners of Legal Entity Customers, together with copies of identifying documentation, and the Company undertakes to provide such additional supporting documentation as the Representatives may reasonably request in connection with the verification of the foregoing certification.

6. (a) The Company represents and agrees that, without the prior consent of the Representatives, it has not made and will not make any offer relating to the Offered Securities that would constitute a "free writing prospectus" as defined in Rule 405 under the Act; each Underwriter represents and agrees that, without the prior consent of the Company and the Representatives, it has not made and will not make any offer relating to the Offered Securities that would constitute a free writing prospectus required to be filed with the Commission; any such free writing prospectus the use of which has been consented to by the Company and the Representatives is listed on Schedule II(a) [or Schedule II(c)] hereto;

(b) The Company has complied and will comply with the requirements of Rule 433 under the Act applicable to any Issuer Free Writing Prospectus, including timely filing with the Commission or retention where required and legending; and the Company represents that it has satisfied and agrees that it will satisfy the conditions under Rule 433 under the Act to avoid a requirement to file with the Commission any electronic road show;

(c) The Company agrees that if at any time following issuance of an Issuer Free Writing Prospectus or Section 5(d) Writing any event occurred or occurs as a result of which such Issuer Free Writing Prospectus or Section 5(d) Writing would conflict with the information in the Registration Statement, the Pricing Prospectus or the Prospectus or would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances then prevailing, not misleading, the Company will give prompt notice thereof to the Representatives and, if requested by the Representatives, will prepare and furnish without charge to each Underwriter an Issuer Free Writing Prospectus, Section 5(d) Writing or other document which will correct such conflict, statement or omission; provided, however, that this representation and warranty shall not apply to any statements or omissions in an Issuer Free Writing Prospectus made in reliance upon and in conformity with the Underwriter Information;

(d) The Company represents and agrees that (i) it has not engaged in, or authorized any other person to engage in, any Section 5(d) Communications, other than Section 5(d) Communications with the prior consent of the Representatives with entities that are qualified institutional buyers as defined in Rule 144A under the Act or institutions that are accredited investors as defined in Rule 501(a) under the Act; and (ii) it has not distributed, or authorized any other person to distribute, any Section 5(d) Writings, other than those distributed with the prior consent of the Representatives that are listed on Schedule III(d) hereto; and the Company reconfirms that the Underwriters have been authorized to act on its behalf in engaging in Section 5(d) Communications;

(e) Each Underwriter represents and agrees that any Section 5(d) Communications undertaken by it were with entities that are qualified institutional buyers as defined in Rule 144A under the Act or institutions that are accredited investors as defined in Rule 501(a) under the Act;

7. The Company covenants and agrees with the several Underwriters that the Company will pay or cause to be paid the following: (i) the fees, disbursements and expenses of the Company's counsel and accountants in connection with the registration of the Offered Securities under the Act and all other expenses in connection with the preparation, printing, reproduction and filing of the Registration Statement, any Preliminary Prospectus, any Section 5(d) Writing, any Issuer Free Writing Prospectus and the Prospectus and amendments and supplements thereto and the mailing and delivering of copies thereof to the Underwriters and dealers; (ii) the cost of printing or producing any agreement among Underwriters, this Agreement, the Deposit Agreement, the Blue Sky Memorandum, closing documents (including any compilations thereof) and any other documents in connection with the offering, purchase, sale and delivery of the Offered Securities; (iii) all expenses in connection with the qualification of the Offered Securities for offering and sale under state securities laws as provided in Section 5(b) hereof, including the fees and disbursements of counsel for the Underwriters in connection with such qualification and in connection with the Blue Sky survey; (iv) all fees and expenses in connection with listing the ADSs on NASDAQ; (v) the filing fees incident to, and the fees and disbursements of counsel for the Underwriters in connection with, any required review by FINRA of the terms of the sale of the ADSs, provided that the reasonable fees and disbursements of counsel to the Underwriters described in this clause (v) shall not exceed $35,000; (vi) the cost of preparing share certificates; (vii) the cost and charges of any transfer agent or registrar; (viii) any Transfer Taxes whether of the UK or any other jurisdiction (including any interest and penalties) payable by the Underwriters or the Company in connection with (a) the issuance and delivery of the Shares by the Company to the Depositary in the manner contemplated by the Deposit Agreement, (b) the issuance and delivery of the ADSs (or the ADRs evidencing the ADSs) by the Depositary to or for the account of the Underwriters in the manner contemplated by this Agreement and the Deposit Agreement, (c) the sale and delivery by the Underwriters of the ADSs to the initial purchasers thereof, (d) the execution and delivery of this Agreement, (e) the grant and/or the

exercise of the option to acquire the Optional ADSs and (f) any other actions taken by the Underwriters with respect to the ADSs that are set forth in the section entitled "Underwriting" in the Prospectus; and (ix) all other costs and expenses incident to the performance of its obligations hereunder which are not otherwise specifically provided for in this Section. It is understood, however, that, except as provided in this Section, and Sections 5(p), 9 and 12 hereof, the Underwriters will pay all of their own costs and expenses, including the fees of their counsel, and any advertising expenses connected with any offers they may make; provided, however, that the Underwriters and the Company shall each pay 50% of the cost of chartering any aircraft to be used in connection with the road show by both the Company and the Underwriters.

8. The obligations of the Underwriters hereunder, as to the ADSs to be delivered at each Time of Delivery, shall be subject, in their discretion, to the condition that all representations and warranties and other statements of the Company herein are, at and as of the Applicable Time and such Time of Delivery, true and correct, the condition that the Company shall have performed all of its obligations hereunder theretofore to be performed, and the following additional conditions:

(a) The Prospectus shall have been filed with the Commission pursuant to Rule 424(b) under the Act within the applicable time period prescribed for such filing by the rules and regulations under the Act and in accordance with Section 5(a) hereof; all material required to be filed by the Company pursuant to Rule 433(d) under the Act shall have been filed with the Commission within the applicable time period prescribed for such filing by Rule 433; if the Company has elected to rely upon Rule 462(b) under the Act, the Rule 462(b) Registration Statement shall have become effective by 10:00 P.M., Washington, D.C. time, on the date of this Agreement; no stop order suspending the effectiveness of the Registration Statement or any part thereof, or the ADS Registration Statement, shall have been issued and no proceeding for that purpose shall have been initiated or threatened by the Commission; no stop order suspending or preventing the use of the Pricing Prospectus, Prospectus, any Issuer Free Writing Prospectus or the ADS Registration Statement shall have been initiated or threatened by the Commission; and all requests for additional information on the part of the Commission shall have been complied with to your reasonable satisfaction;

(b) Cooley LLP, counsel for the Underwriters, shall have furnished to you such written opinion or opinions, dated such Time of Delivery, in form and substance satisfactory to the Representatives, with respect to such matters as the Representatives may reasonably request, and such counsel shall have received such papers and information as they may reasonably request to enable them to pass upon such matters;

(c) Goodwin Procter LLP, U.S. counsel for the Company, shall have furnished to the Representatives their written opinion and negative assurance letter, dated such Time of Delivery, in form and substance satisfactory to you;

(d) Goodwin Procter (UK) LLP, English counsel for the Company, shall have furnished to the Representatives their written opinion and negative assurance letter, dated such Time of Delivery, in form and substance satisfactory to you;

(e) Each of (i) Dechert LLP, (ii) Maschio and Soames IP Limited and (iii) Sagittarius IP, each intellectual property counsel for the Company, shall have furnished to the Representatives their written opinions, dated such Time of Delivery, in form and substance satisfactory to you;

(f) Patterson Belknap Webb & Tyler LLP, counsel for the Depositary, shall have furnished to you their written opinion, dated such Time of Delivery, in form and substance satisfactory to you;

(g) On the date of the Prospectus at a time prior to the execution of this Agreement, at 9:30 a.m., New York City time, on the effective date of any post-effective amendment to the Registration Statement filed subsequent to the date of this Agreement and also at each Time of Delivery, PricewaterhouseCoopers LLP shall have furnished to the Representatives a letter or letters, dated the respective dates of delivery thereof, in form and substance satisfactory to the Representatives;

(h) (i) Neither the Company nor any of its subsidiaries shall have sustained since the date of the latest audited financial statements included in the Pricing Prospectus and the Prospectus any loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree, otherwise than as set forth or contemplated in the Pricing Prospectus and the Prospectus, and (ii) since the respective dates as of which information is given in the Pricing Prospectus and the Prospectus there shall not have been any change in the capital stock (other than as a result of the exercise of stock options or the award of stock options or restricted stock in the ordinary course of business pursuant to the Company's equity plans that are described in the Pricing Prospectus) or long-term debt of the Company or any of its subsidiaries or any change or effect, or any development involving a prospective change or effect, in or affecting (x) the business, properties, general affairs, management, financial position, shareholders' equity or results of operations of the Company and its subsidiaries, taken as a whole, except as set forth or contemplated in the Pricing Prospectus and the Prospectus, or (y) the ability of the Company to perform its obligations under this Agreement, including the issuance and sale of the ADSs, or to consummate the transactions contemplated in the Pricing Prospectus and the Prospectus, the effect of which, in any such case described in clause (i) or (ii), is in your judgment so material and adverse as to make it impracticable or inadvisable to proceed with the public offering or the delivery of the ADSs being delivered at such Time of Delivery

on the terms and in the manner contemplated in the Pricing Prospectus and the Prospectus;

(i) On or after the Applicable Time (i) no downgrading shall have occurred in the rating accorded the Company's debt securities by any "nationally recognized statistical rating organization", as that term is defined by the Commission for purposes of Rule 436(g)(2) under the Act, and (ii) no such organization shall have publicly announced that it has under surveillance or review, with possible negative implications, its rating of any of the Company's debt securities;

(j) On or after the Applicable Time there shall not have occurred any of the following: (i) a suspension or material limitation in trading in securities generally on the New York Stock Exchange or on the NASDAQ; (ii) a suspension or material limitation in trading in the Company's securities on the NASDAQ; (iii) a general moratorium on commercial banking activities declared by either Federal, Massachusetts State or New York State authorities or a material disruption in commercial banking or securities settlement or clearance services in the United States or the United Kingdom; (iv) the outbreak or escalation of hostilities involving the United States or the United Kingdom or the declaration by the United States or the United Kingdom of a national emergency or war or (v) the occurrence of any other calamity or crisis or any change in financial, political or economic conditions in the United States, the United Kingdom or elsewhere, if the effect of any such event specified in clause (iv) or (v) in your judgment makes it impracticable or inadvisable to proceed with the public offering or the delivery of the ADSs being delivered at such Time of Delivery on the terms and in the manner contemplated in the Pricing Prospectus and the Prospectus;

(k) The Depositary shall have furnished or caused to be furnished to the Representatives at such Time of Delivery, (a) certificates satisfactory to the Representatives evidencing the deposit with it of the Shares being so deposited against issuance of ADSs and ADRs evidencing the ADSs to be delivered by the Company at such Time of Delivery, and (b) the execution, countersignature (if applicable), issuance and delivery of ADSs and ADRs evidencing such ADSs pursuant to the Deposit Agreement;

(l) The ADSs to be sold at such Time of Delivery shall have been duly listed on the NASDAQ;

(m) The Company shall have obtained and delivered to the Underwriters executed copies of a lock-up agreement from each director, officer and other security holder of the Company representing all of the share capital of the Company, substantially to the effect set forth in Annex II hereof in form and substance satisfactory to the Representatives;

(n) The Company shall have delivered to the Representatives on the date of the Prospectus at a time prior to the execution of this Agreement and at such

Time of Delivery a certificate of the Chief Financial Officer of the Company, in form and substance satisfactory to you;

(o) The Company shall have complied with the provisions of Section 5(c) hereof with respect to the furnishing of prospectuses on the New York Business Day next succeeding the date of this Agreement; and

(p) The Company shall have furnished or caused to be furnished to you at such Time of Delivery certificates of officers of the Company satisfactory to you as to the accuracy of the representations and warranties of the Company herein at and as of such Time of Delivery, as to the performance by the Company of all of its obligations hereunder to be performed at or prior to such Time of Delivery, as to the matters set forth in subsections (a) and (e) of this Section and as to such other matters as you may reasonably request.

9. (a) The Company will indemnify and hold harmless each Underwriter against any losses, claims, damages or liabilities, joint or several, to which such Underwriter may become subject, under the Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon an untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, any Issuer Free Writing Prospectus, any "roadshow" as defined in Rule 433(h) under the Act (a "roadshow"), any "issuer information" filed or required to be filed pursuant to Rule 433(d) under the Act, or any Section 5(d) Writing, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, and will reimburse each Underwriter for any legal or other expenses reasonably incurred by such Underwriter in connection with investigating or defending any such action or claim as such expenses are incurred; *provided*, *however*, that the Company shall not be liable in any such case to the extent that any such loss, claim, damage or liability arises out of or is based upon an untrue statement or alleged untrue statement or omission or alleged omission made in the Registration Statement, the ADS Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, any road show, or any Section 5(d) Writing, in reliance upon and in conformity with the Underwriter Information.

(b) Each Underwriter, severally and not jointly, will indemnify and hold harmless the Company against any losses, claims, damages or liabilities to which the Company may become subject, under the Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon an untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, the ADS Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, or any

roadshow or any Section 5(d) Writing, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in each case to the extent, but only to the extent, that such untrue statement or alleged untrue statement or omission or alleged omission was made in the Registration Statement, the ADS Registration Statement, any Preliminary Prospectus, the Pricing Prospectus or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, or any roadshow or any Section 5(d) Writing, in reliance upon and in conformity with the Underwriter Information; and will reimburse the Company for any legal or other expenses reasonably incurred by the Company in connection with investigating or defending any such action or claim as such expenses are incurred. As used in this Agreement with respect to an Underwriter and an applicable document, "Underwriter Information" shall mean the written information furnished to the Company by such Underwriter through the Representatives expressly for use therein; it being understood and agreed upon that the only such information furnished by any Underwriter consists of the following information in the Prospectus furnished on behalf of each Underwriter: the concession and reallowance figures appearing in the fifth paragraph under the caption "Underwriting", and the information contained in the tenth, eleventh and twelfth paragraphs under the caption "Underwriting"

(c) Promptly after receipt by an indemnified party under subsection (a) or (b) of this Section 9 of notice of the commencement of any action, such indemnified party shall, if a claim in respect thereof is to be made against the indemnifying party under such subsection, notify the indemnifying party in writing of the commencement thereof; provided that the failure to notify the indemnifying party shall not relieve it from any liability that it may have under the preceding paragraphs of this Section 9 except to the extent that it has been materially prejudiced (through the forfeiture of substantive rights or defenses) by such failure; and provided further that the failure to notify the indemnifying party shall not relieve it from any liability that it may have to an indemnified party otherwise than under the preceding paragraphs of this Section 9. In case any such action shall be brought against any indemnified party and it shall notify the indemnifying party of the commencement thereof, the indemnifying party shall be entitled to participate therein and, to the extent that it shall wish, jointly with any other indemnifying party similarly notified, to assume the defense thereof, with counsel satisfactory to such indemnified party (who shall not, except with the consent of the indemnified party, be counsel to the indemnifying party), and, after notice from the indemnifying party to such indemnified party of its election so to assume the defense thereof, the indemnifying party shall not be liable to such indemnified party under such subsection for any legal expenses of other counsel or any other expenses, in each case subsequently incurred by such indemnified party, in connection with the defense thereof other than reasonable costs of investigation. No indemnifying party shall, without the written consent of the indemnified party, effect the settlement or compromise of, or consent to the entry of any judgment with respect to, any pending or threatened action or claim in respect of which indemnification or contribution may be sought hereunder (whether or not the indemnified party is an actual or potential party to

such action or claim) unless such settlement, compromise or judgment (i) includes an unconditional release of the indemnified party from all liability arising out of such action or claim and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act, by or on behalf of any indemnified party.

(d) If the indemnification provided for in this Section 9 is unavailable to or insufficient to hold harmless an indemnified party under subsection (a) or (b) above in respect of any losses, claims, damages or liabilities (or actions in respect thereof) referred to therein, then each indemnifying party shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities (or actions in respect thereof) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the ADSs. If, however, the allocation provided by the immediately preceding sentence is not permitted by applicable law, then each indemnifying party shall contribute to such amount paid or payable by such indemnified party in such proportion as is appropriate to reflect not only such relative benefits but also the relative fault of the Company on the one hand and the Underwriters on the other in connection with the statements or omissions which resulted in such losses, claims, damages or liabilities (or actions in respect thereof), as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other shall be deemed to be in the same proportion as the total net proceeds from the offering (before deducting expenses) received by the Company bear to the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover page of the Prospectus. The relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or the Underwriters on the other and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to this subsection (d) were determined by *pro rata* allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this subsection (d). The amount paid or payable by an indemnified party as a result of the losses, claims, damages or liabilities (or actions in respect thereof) referred to above in this subsection (d) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this subsection (d), no Underwriter shall be required to contribute any amount in excess of the amount by which the total price at which the ADSs underwritten by it and distributed to the public were offered to the public exceeds the amount of any damages which such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) shall be entitled to contribution from any person who was not guilty of such fraudulent

misrepresentation. The Underwriters' obligations in this subsection (d) to contribute are several in proportion to their respective underwriting obligations and not joint.

(e) The obligations of the Company under this Section 9 shall be in addition to any liability which the Company may otherwise have and shall extend, upon the same terms and conditions, to each employee, officer and director of each Underwriter and each person, if any, who controls any Underwriter within the meaning of the Act and each broker-dealer affiliate of any Underwriter; and the obligations of the Underwriters under this Section 9 shall be in addition to any liability which the respective Underwriters may otherwise have and shall extend, upon the same terms and conditions, to each officer and director of the Company (including any person who, with his or her consent, is named in the Registration Statement as about to become a director of the Company) and to each person, if any, who controls the Company within the meaning of the Act.

10. (a) If any Underwriter shall default in its obligation to purchase the ADSs which it has agreed to purchase hereunder at a Time of Delivery, you may in your discretion arrange for you or another party or other parties to purchase such ADSs on the terms contained herein. If within thirty-six hours after such default by any Underwriter you do not arrange for the purchase of such ADSs, then the Company shall be entitled to a further period of thirty-six hours within which to procure another party or other parties satisfactory to you to purchase such ADSs on such terms. In the event that, within the respective prescribed periods, you notify the Company that you have so arranged for the purchase of such ADSs, or the Company notifies you that it has so arranged for the purchase of such ADSs, you or the Company shall have the right to postpone such Time of Delivery for a period of not more than seven days, in order to effect whatever changes may thereby be made necessary in the Registration Statement or the Prospectus, or in any other documents or arrangements, and the Company agrees to file promptly any amendments or supplements to the Registration Statement or the Prospectus which in your opinion may thereby be made necessary. The term "Underwriter" as used in this Agreement shall include any person substituted under this Section with like effect as if such person had originally been a party to this Agreement with respect to such ADSs.

(b) If, after giving effect to any arrangements for the purchase of the ADSs of a defaulting Underwriter or Underwriters by you and the Company as provided in subsection (a) above, the aggregate number of such ADSs which remains unpurchased does not exceed one-eleventh of the aggregate number of all the ADSs to be purchased at such Time of Delivery, then the Company shall have the right to require each non-defaulting Underwriter to purchase the number of ADSs which such Underwriter agreed to purchase hereunder at such Time of Delivery and, in addition, to require each non-defaulting Underwriter to purchase its pro rata share (based on the number of ADSs which such Underwriter agreed to purchase hereunder) of the ADSs of such defaulting Underwriter or Underwriters for which such arrangements have not been made; but nothing herein shall relieve a defaulting Underwriter from liability for its default.

(c) If, after giving effect to any arrangements for the purchase of the ADSs of a defaulting Underwriter or Underwriters by you and the Company as provided in subsection (a) above, the aggregate number of such ADSs which remains unpurchased exceeds one-eleventh of the aggregate number of all the ADSs to be purchased at such Time of Delivery, or if the Company shall not exercise the right described in subsection (b) above to require non-defaulting Underwriters to purchase ADSs of a defaulting Underwriter or Underwriters, then this Agreement (or, with respect to the Second Time of Delivery, the obligations of the Underwriters to purchase and of the Company to sell the Optional ADSs) shall thereupon terminate, without liability on the part of any non-defaulting Underwriter or the Company, except for the expenses to be borne by the Company and the Underwriters as provided in Section 7 hereof and the indemnity and contribution agreements in Section 9 hereof; but nothing herein shall relieve a defaulting Underwriter from liability for its default.

11. The respective indemnities, rights of contribution, agreements, representations, warranties and other statements of the Company and the several Underwriters, as set forth in this Agreement or made by or on behalf of them, respectively, pursuant to this Agreement, shall remain in full force and effect, regardless of any investigation (or any statement as to the results thereof) made by or on behalf of any Underwriter or any controlling person of any Underwriter, or the Company, or any officer or director or controlling person of the Company, and shall survive delivery of and payment for the ADSs.

12. If this Agreement shall be terminated pursuant to Section 10 hereof, the Company shall not then be under any liability to any Underwriter except as provided in Sections 7 and 9 hereof; but, if for any other reason, any ADSs are not delivered by or on behalf of the Company as provided herein, the Company will reimburse the Underwriters through you for all out-of-pocket expenses approved in writing by you, including fees and disbursements of counsel, reasonably incurred by the Underwriters in making preparations for the purchase, sale and delivery of the ADSs not so delivered, but the Company shall then be under no further liability to any Underwriter except as provided in Sections 7 and 9 hereof.

13. In all dealings hereunder, you shall act on behalf of each of the Underwriters, and the parties hereto shall be entitled to act and rely upon any statement, request, notice or agreement on behalf of any Underwriter made or given by you jointly or by the Representatives on behalf of the Underwriters.

All statements, requests, notices and agreements hereunder shall be in writing, and (A) if to the Underwriters shall be delivered or sent by mail, telex or facsimile transmission to you as the representatives (i) in care of Goldman Sachs & Co. LLC, 200 West Street, New York, New York 10282-2198, Attention: Registration Department; (ii) in care of Jefferies LLC, 520 Madison Avenue, New York, New York 10022, Attention: General Counsel; and (iii) in care of Piper Jaffray & Co., 800 Nicollet Mall, Minneapolis, Minnesota 55402, to the attention of Equity Capital Markets and separately, General Counsel; and (B) if to the

Company shall be delivered or sent by mail, telex or facsimile transmission to the address of the Company set forth on the cover of the Registration Statement, Attention: Secretary; provided, however, that any notice to an Underwriter pursuant to Section 9(c) hereof shall be delivered or sent by mail, telex or facsimile transmission to such Underwriter at its address set forth in its Underwriters' Questionnaire, or telex constituting such Questionnaire, which address will be supplied to the Company by you upon request. Any such statements, requests, notices or agreements shall take effect upon receipt thereof.

In accordance with the requirements of the USA Patriot Act (Title III of Pub. L. 107-56 (signed into law October 26, 2001)), the Underwriters are required to obtain, verify and record information that identifies their respective clients, including the Company, which information may include the name and address of their respective clients, as well as other information that will allow the Underwriters to properly identify their respective clients.

14. This Agreement shall be binding upon, and inure solely to the benefit of, the Underwriters, the Company and, to the extent provided in Sections 9 and 11 hereof, the officers and directors of the Company and each person who controls the Company or any Underwriter, and their respective heirs, executors, administrators, successors and assigns, and no other person shall acquire or have any right under or by virtue of this Agreement. No purchaser of any of the ADSs from any Underwriter shall be deemed a successor or assign by reason merely of such purchase.

15. Time shall be of the essence of this Agreement. As used herein, the term "business day" shall mean any day when the Commission's office in Washington, D.C. is open for business.

16. The Company acknowledges and agrees that (i) the purchase and sale of the ADSs pursuant to this Agreement is an arm's-length commercial transaction between the Company, on the one hand, and the several Underwriters, on the other, (ii) in connection therewith and with the process leading to such transaction each Underwriter is acting solely as a principal and not the agent or fiduciary of the Company, (iii) no Underwriter has assumed an advisory or fiduciary responsibility in favor of the Company with respect to the offering contemplated hereby or the process leading thereto (irrespective of whether such Underwriter has advised or is currently advising the Company on other matters) or any other obligation to the Company except the obligations expressly set forth in this Agreement and (iv) the Company has consulted its own legal and financial advisors to the extent it deemed appropriate. The Company agrees that it will not claim that the Underwriters, or any of them, has rendered advisory services of any nature or respect, or owes a fiduciary or similar duty to the Company, in connection with such transaction or the process leading thereto.

17. This Agreement supersedes all prior agreements and understandings (whether written or oral) between the Company and the Underwriters, or any of them, with respect to the subject matter hereof.

18. This Agreement and any transaction contemplated by this Agreement shall be governed by and construed in accordance with the laws of the State of New York without regard to principles of conflict of laws that would results in the application of any other law than the laws of the State of New York. The Company agrees that any suit or proceeding arising in respect of this Agreement or any transaction contemplated by this Agreement will be tried exclusively in the U.S. District Court for the Southern District of New York or, if that court does not have subject matter jurisdiction, in any state court located in The City and County of New York and the Company agrees to submit to the jurisdiction of, and to venue in, such courts. The Company hereby irrevocably appoints [·], as its authorized agent upon which process may be served in any suit or proceeding arising out of or relating to this Agreement or the transactions contemplated hereby, and the Company agrees to take any and all action as may be necessary to maintain such designation and appointment of such agent in full force and effect for a period of seven years from the date of this Agreement.

19. The Company and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

20. Solely for the purposes of the requirements of Article 9(8) of the MIFID Product Governance rules under EU Delegated Directive 2017/593 (the "Product Governance Rules") regarding the mutual responsibilities of manufacturers under the Product Governance Rules:

(a) each manufacturer acknowledges to each other manufacturer that it understands the responsibilities conferred upon it under the Product Governance Rules relating to each of the product approval process, the target market and the eligible distribution channels for dissemination of the ADSs and the related information set out in the Prospectus in connection with the ADSs; and

(b) the Representatives and the Company note the application of the Product Governance Rules and acknowledge the target market and distribution channels identified as applying to the ADSs by the manufacturers and the related information set out in the Prospectus in connection with the ADSs.

21. This Agreement may be executed by any one or more of the parties hereto in any number of counterparts, each of which shall be deemed to be an original, but all such counterparts shall together constitute one and the same instrument.

22. Notwithstanding anything herein to the contrary, the Company is authorized to disclose to any persons the U.S. federal and state income tax treatment and tax

structure of the potential transaction and all materials of any kind (including tax opinions and other tax analyses) provided to the Company relating to that treatment and structure, without the Underwriters imposing any limitation of any kind. However, any information relating to the tax treatment and tax structure shall remain confidential (and the foregoing sentence shall not apply) to the extent necessary to enable any person to comply with securities laws. For this purpose, "tax structure" is limited to any facts that may be relevant to that treatment.

23. Recognition of the U.S. Special Resolution Regimes.

(a) In the event that any Underwriter that is a Covered Entity becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from such Underwriter of this Agreement, and any interest and obligation in or under this Agreement, will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United States.

(b) In the event that any Underwriter that is a Covered Entity or a BHC Act Affiliate of such Underwriter becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against such Underwriter are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed.

(c) As used in this section:

"BHC Act Affiliate" has the meaning assigned to the term "affiliate" in, and shall be interpreted in accordance with, 12 U.S.C. § 1841(k).

"Covered Entity" means any of the following:

(i) a "covered entity" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b);

(ii) a "covered bank" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or

(iii) a "covered FSI" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b).

"Default Right" has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable.

"U.S. Special Resolution Regime" means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

[Signature Page Follows]

If the foregoing is in accordance with your understanding, please sign and return to us one for the Company and each of the Representatives plus one for each counsel counterparts hereof, and upon the acceptance hereof by you, on behalf of each of the Underwriters, this letter and such acceptance hereof shall constitute a binding agreement between each of the Underwriters and the Company. It is understood that your acceptance of this letter on behalf of each of the Underwriters is pursuant to the authority set forth in a form of agreement among Underwriters, the form of which shall be submitted to the Company for examination upon request, but without warranty on your part as to the authority of the signers thereof.

Very truly yours,

Bicycle Therapeutics plc

By:
Name:
Title:

Accepted as of the date hereof:

Goldman Sachs & Co. LLC

By:
Name:
Title:

Jefferies LLC

By:
Name:
Title:

Piper Jaffray & Co.

By:
Name:
Title:

On behalf of each of the Underwriters

[Signature Page to Underwriting Agreement]

SCHEDULE I

Underwriter	Total Number of Firm ADSs to be Purchased	Number of Optional ADSs to be Purchased if Maximum Option Exercised
Goldman Sachs & Co. LLC	[·]	[·]
Jefferies LLC	[·]	[·]
Piper Jaffray & Co.	[·]	[·]
Canaccord Genuity LLC	[·]	[·]
Total	[·]	[·]

SCHEDULE II

(a) Issuer Free Writing Prospectuses not included in the Pricing Disclosure Package:

[Electronic roadshow dated [·]]

(b) Additional Documents Incorporated by Reference:

[None]

(c) Information other than the Pricing Prospectus that comprise the Pricing Disclosure Package:

The initial public offering price per ADS for the ADSs is $[·]
The number of ADSs purchased by the Underwriters is [·].

[Add any other pricing disclosure.]

(d) Section 5(d) Writings:

[·]

ANNEX I

[Form of Press Release]

Bicycle Therapeutics plc
[Date]

Bicycle Therapeutics plc (the "Company") announced today that Goldman Sachs & Co. LLC, Jefferies LLC and Piper Jaffray & Co., the lead book-running managers in the Company's recent public sale of ADSs, are [waiving] [releasing] a lock-up restriction with respect to ordinary shares held by [certain officers or directors] [an officer or director] of the Company. The [waiver] [release] will take effect on ,20 , and the shares may be sold on or after such date.

This press release is not an offer for sale of the securities in the United States or in any other jurisdiction where such offer is prohibited, and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the United States Securities Act of 1933, as amended.

ANNEX II

[Form of Lock-Up Agreement]

Bicycle Therapeutics Limited

Lock-Up Agreement

[·], 2018

Goldman Sachs & Co. LLC
Jefferies LLC
Piper Jaffray & Co.

As representatives of the several Underwriters
named in Schedule I hereto

c/o Goldman Sachs & Co. LLC
200 West Street
New York, NY 10282-2198

c/o Jefferies LLC
520 Madison Avenue
New York, NY 10022

c/o Piper Jaffray & Co.
345 Park Avenue, 12th Floor
New York, NY 10154

Re: Bicycle Therapeutics Limited - Lock-Up Agreement

Ladies and Gentlemen:

The undersigned understands that you, as representatives (the "**Representatives**"), propose to enter into an Underwriting Agreement on behalf of the several Underwriters named in Schedule I to such agreement (collectively, the "**Underwriters**"), providing for a public offering of the equity securities (the "**Public Offering**"), whether in the form of ordinary shares or otherwise (the "**Shares**") of Bicycle Therapeutics Limited, a private limited company organized under the laws of England and Wales ("**Bicycle Limited**"), or of an entity resulting from, or which becomes the ultimate parent company that owns, directly or indirectly, 100% of the outstanding voting securities of Bicycle Limited as a result of, any reorganization, conversion or other restructuring, including by way of a merger or other business combination transaction, or that is a successor in interest to Bicycle Limited (with Bicycle Limited or such ultimate parent entity, as the case may be, being referred to as the "**Company**," and the

outstanding voting securities of the Company being referred to as the "**Equity Securities**"), pursuant to a Registration Statement on Form S-1 to be filed with the Securities and Exchange Commission (the "**SEC**").

In consideration of the agreement by the Underwriters to offer and sell the Shares, and of other good and valuable consideration the receipt and sufficiency of which is hereby acknowledged, the undersigned agrees that, during the period beginning from the date of this Lock-Up Agreement and continuing to and including the date 180 days after the date set forth on the final prospectus used to sell the Shares (the "**Lock-Up Period**"), the undersigned will not offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of any Equity Securities of the Company, or any options or warrants to purchase any Equity Securities of the Company, or any securities convertible into, exchangeable for or that represent the right to receive Equity Securities of the Company, whether now owned or hereinafter acquired, owned directly by the undersigned (including holding as a custodian) or with respect to which the undersigned has beneficial ownership within the rules and regulations of the SEC (collectively the "**Undersigned's Securities**"). The foregoing restriction is expressly agreed to preclude the undersigned from engaging in any hedging or other transaction which is designed to or which reasonably could be expected to lead to or result in a sale or disposition of the Undersigned's Securities even if such Undersigned's Securities would be disposed of by someone other than the undersigned. Such prohibited hedging or other transactions would include without limitation any short sale or any purchase, sale or grant of any right (including without limitation any put or call option) with respect to any of the Undersigned's Securities or with respect to any security that includes, relates to, or derives any significant part of its value from such Undersigned's Securities. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed Shares the undersigned may purchase in the Public Offering ("**Issuer Directed Shares**"). In addition, the undersigned agrees that, without the prior written consent of the Representatives on behalf of the Underwriters, it will not, during the Lock-Up Period, make any demand for or exercise any right with respect to, the registration of any Equity Securities or any security convertible into or exercisable or exchangeable for Equity Securities.

If the undersigned is an officer or director of the Company, (i) the Representatives agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of Equity Securities, the Representatives will notify the Company of the impending release or waiver, and (ii) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (a) the release or waiver is effected solely to permit a transfer not for consideration and (b) the transferee has agreed in writing to be bound by the same terms described in this letter to the extent and for the duration that such terms remain in effect at the time of the transfer.

Notwithstanding the foregoing, the undersigned may transfer or dispose of the Undersigned's Securities

(i) as a *bona fide* gift or gifts, provided that the donee or donees thereof agree to be bound in writing by the restrictions set forth herein,

(ii) to any immediate family member of the undersigned or any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned, provided that the immediate family member or trustee of the trust agrees to be bound in writing by the restrictions set forth herein, and provided further that any such transfer shall not involve a disposition for value; provided, further, that no filing under the Securities Exchange Act of 1934, as amended (the "**Exchange Act**") or other public announcement shall be required or voluntarily made in connection with such transfer during the Lock-Up Period,

(iii) by will or intestate succession upon the death of the undersigned, provided that each recipient agrees to be bound in writing by the restrictions set forth herein, and provided further that any filing made pursuant to Section 16(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), shall include a footnote noting the circumstances described in this clause,

(iv) by operation of law or by order of a court of competent jurisdiction pursuant to a qualified domestic order or in connection with a divorce settlement, provided that each recipient agrees to be bound in writing by the restrictions set forth herein, and provided, further, that any filing made pursuant to Section 16(a) of the Exchange Act, shall include a footnote noting the circumstances described in this clause,

(v) if the undersigned is a non-individual, to any affiliate (as such term is defined in Rule 405 of the Securities Act of 1933), limited partners, member, stockholder or other equity holders or trust beneficiaries of the undersigned or to any investment fund or other entity controlled or managed by the undersigned, provided that any such transferee agrees to be bound in writing by the restrictions set forth herein and such transfer or disposition is not for value, and provided further that no filing under the Exchange Act or other public announcement shall be required or voluntarily made in connection with such transfer during the Lock-Up Period,

(vi) that are acquired in the Public Offering (other than Issuer-Directed Shares) or in transactions relating to the Equity Securities acquired in open market transactions after the date of the final prospectus, provided that no public announcement or filing under the Exchange Act, other than any required filing on Schedule 13G, Schedule 13G/A or Form 13F, shall be required or voluntarily made by the undersigned in connection with such transfer during the Lock-up Period,

(vii) pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of the Equity Securities involving a Change of Control (as defined below) of the Company after the closing of the Public Offering and approved by the

Company's board of directors, provided that in the event that the tender offer, merger, consolidation or other such transaction is not completed, the Undersigned's Securities shall remain subject to the restrictions contained in this agreement,

(viii) to the Company in connection with the repurchase of the Undersigned's Securities with the termination of the undersigned's employment or other service with the Company, or to cover tax withholding obligations in connection with the exercise of options or warrants or for the primary purpose of paying the exercise price of options or warrants to acquire Equity Securities, in each case pursuant to a share option or other plan or arrangement, or warrants existing as of the date hereof or described in the final prospectus, provided that if the undersigned is required to file a report under the Exchange Act related thereto, such report shall include a footnote noting the circumstances described in this clause,

(ix) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (i), (ii), (iii), (v)above; or

(x) with the prior written consent of the Representatives on behalf of the Underwriters.

For purposes of this Lock-Up Agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin, and "Change in Control" shall mean the consummation of any bona fide third party tender offer, merger, amalgamation, consolidation or other similar transaction the result of which is that any "person" (as defined in Section 13(d)(3) of the Exchange Act), or group of persons, other than the Company, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of 90% of the total voting power of the voting shares of the Company.

In addition, notwithstanding the foregoing, if the undersigned is a corporation, the corporation may transfer the capital stock of the Company to any wholly-owned subsidiary of such corporation; provided, however, that in any such case, it shall be a condition to the transfer that the transferee execute an agreement stating that the transferee is receiving and holding such capital stock subject to the provisions of this Agreement and there shall be no further transfer of such capital stock except in accordance with this Agreement, and provided further that any such transfer shall not involve a disposition for value.

The undersigned now has, and, except as contemplated by the terms hereof, for the duration of this Lock-Up Agreement will have, good and marketable title to the Undersigned's Securities, free and clear of all liens, encumbrances, and claims whatsoever. The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Undersigned's Securities except in compliance with the foregoing restrictions.

In addition, the undersigned may enter into any plan designed to satisfy the requirements of Rule 10b5-1 (a "10b5-1 Plan") under the Exchange Act (other than the entry into such a plan in such a manner as to allow the sale of Equity Securities, in each case, within the Lock-Up Period); provided however, no sale of Equity Securities may be made under such

10b5-1 Plan during the Lock-Up Period and no public announcement or filing under the Exchange Act regarding the establishment of such 10b5-1 Plan shall be required or made during the Lock-Up Period.

In the event that, during the Lock-up Period, the Representatives grant a discretionary release or waiver of Equity Securities to (i) an officer or director of the Company or (ii) any shareholder of the Company who has executed and delivered to the Representatives a copy of this agreement and beneficially owns (as such term is defined in Rule 13d-3 under the Exchange Act) 1.0% or more of the outstanding Equity Securities, calculated as of the closing of the Public Offering (each, a "Released Party"), then the Representatives shall be deemed to have also released or waived, on the same terms and conditions, if any, the prohibitions set forth in this agreement that would otherwise have applied to the undersigned on a pro-rata basis with respect to the same proportion (determined as a percentage) of the Undersigned's Securities as (x) the aggregate amount of Equity Securities of the Released Party subject to the release or waiver bears to (y) the aggregate amount of shares of Equity Securities held by the Released Party at the time of the release or waiver. The provisions of this paragraph will not apply: (i) unless and until the Representatives have first released or waived more than 2.0% (determined as of the date of such waiver) of the Equity Securities in the aggregate from such prohibitions; (ii) (a) if the release or waiver is effected solely to permit a transfer not involving a disposition for value and (b) the transferee has agreed in writing to be bound by the same terms described in this agreement for the duration of the Lock-up Period; (iii) with respect to any release granted by the Representatives to a director or officer of the Company due to financial hardship, as determined by the Representatives in their sole discretion or (iv) if the release or waiver is granted to a holder of Equity Securities in connection with an underwritten public offering, whether or not such offering is wholly or partially a secondary offering, of Equity Securities pursuant to a registration statement under the Securities Act. In the event that, as a result of this paragraph, any Equity Securities held by the undersigned are to be released or waived from the restrictions imposed by this agreement, the Representatives shall use commercially reasonable efforts to notify the Company two business days prior to the effective date of such release or waiver, and the Company, in turn, shall use commercially reasonable efforts notify the undersigned within one business day thereafter that the same percentage of aggregate Equity Securities held by the undersigned has been released or waived from the restrictions set forth in this agreement; provided, that the failure to give any such notice to the Company or the undersigned shall not give rise to any claim or liability against the Underwriters, including the Representatives.

Notwithstanding anything to the contrary contained herein, this Lock-Up Agreement will automatically terminate and the undersigned will be released from all of his, her or its obligations hereunder upon the earliest to occur, if any, of (i) prior to the execution of the Underwriting Agreement, the Company advises the Representatives in writing that it has determined not to proceed with the Public Offering of the Equity Securities, (ii) the date on which the Company files an application to withdraw the registration statement related to the Public Offering, (ii) the Underwriting Agreement is executed but is terminated (other than the

provisions thereof which survive termination) prior to payment for and delivery of the Equity Securities to be sold thereunder, or (iv) May 31, 2019, in the event that the Underwriting Agreement has not been executed by such date; provided, however, that the Company may, by written notice to you prior to such date, extend such date for a period of up to three additional months.

The undersigned understands that the Company and the Underwriters are relying upon this Lock-Up Agreement in proceeding toward consummation of the Public Offering. The undersigned further understands that this Lock-Up Agreement is irrevocable and shall be binding upon the undersigned's heirs, legal representatives, successors, and assigns.

Very truly yours,

_____

Name of Security Holder *(Print exact name*)

By: _____

Signature

If not signing in an individual capacity:

_____

Name of Authorized Signatory *(Print*)

_____

Title of Authorized Signatory *(Print*)

(indicate capacity of person signing if signing as custodian, trustee, or on behalf of an entity)

Exhibit 3.1

THE COMPANIES ACT 2006

COMPANY LIMITED BY SHARES

ARTICLES OF ASSOCIATION

OF

BICYCLE THERAPEUTICS LIMITED

Company number: 11036004

(Adopted by a written resolution passed on 21 December 2018)

THE COMPANIES ACT 2006

COMPANY LIMITED BY SHARES

ARTICLES OF ASSOCIATION

OF

BICYCLE THERAPEUTICS LIMITED

(Adopted by a written resolution passed on 21 December 2018)

1. INTRODUCTION

1.1 The Regulations contained or incorporated in Table A in the Schedule to the Companies (Tables A to F) Regulations 1985 as amended by:

(a) The Companies (Tables A to F) Amendment Regulations 1985;

(b) Schedule 1 to the Companies Act 1985 (Electronic Communications) Order 2000 (SI 2000/3373);

(c) The Companies (Table A to F) (Amendment) Regulations 2007 (SI 2007/2541); and

(d) The Companies (Tables A to F) (Amendment) (No. 2) Regulations 2007 (SI 2007/2826),

("**Table A**") shall apply to the Company, save insofar as they are varied or excluded by, or are inconsistent with, the following Articles.

1.2 In Regulation 1 of Table A, the words "*and in articles of association adopting the same" shall be inserted after the word "regulations*" in the last paragraph of that Regulation and the sentence "*Any reference to any statutory provision shall be deemed to include a reference to each and every statutory amendment, modification, re-enactment and extension thereof for the time being in force*" shall be inserted at the end of that Regulation.

1.3 In these Articles:

(a) article headings are used for convenience only and shall not affect the construction or interpretation of these Articles;

(b) words denoting the singular include the plural and vice versa and reference to one gender includes the other gender and neuter and vice versa; and

(c) Regulations 8, 29, 30, 31, 54, 62, 76, 77, 82, 94 to 98 (inclusive) 115 and 118 of Table A shall not apply to the Company.

1.4 In respect of any actions or matters requiring the acceptance, approval, agreement, consent or words having similar effect of an Investor Director under these Articles, if at any time the Investor Director in question has not been appointed or the Investor Director declares in writing to the Company and the person referred to in Articles 25.1 to 25.7 appointing him (his "**Appointor**") that he considers that providing (or withholding) such acceptance,

approval, agreement or consent gives rise or may give rise to a conflict of interest to his duties as a Director, such action or matter shall require the consent of his Appointor or, in the case of the CIC Director, the CIC Group Representative (acting on behalf of CIC and/or its Permitted Transferees, as the case may be).

2. DEFINITIONS

2.1 In these Articles the following words and expressions shall have the following meanings:

2006 Act	the Companies Act 2006 (as amended from time to time);
A Ordinary Conversion Rate	the conversion rate of one A Ordinary Share into one Ordinary Share, subject to adjustment in accordance with Article 8.8;
A Ordinary Issue Price	in respect of each A Ordinary Share: (a) in issue at the Date of Adoption, £10 per A Ordinary Share; and (b) issued after the Date of Adoption, the price at which the relevant A Ordinary Share is issued including any premium, subject to the appropriate proportionate adjustment following any Capital Reorganisation;
A Ordinary Shares	the A ordinary shares of £0.01 each in the capital of the Company;
A Ordinary Shareholders	the holders of the A Ordinary Shares;
Acting in Concert	has the meaning given to it in The City Code on Takeovers and Mergers published by the Panel on Takeovers and Mergers (as amended from time to time);
Actions	shall have the meaning given to the term in Article 6.2;
Ahren	Ahren LP, a private fund limited partnership registered in England and Wales whose registered office is at 15 Queens Grove, London, United Kingdom, NW8 6EL;
As Converted Basis	in reference to any calculation or number, means that such calculation shall be made, or number determined, on the basis that each Preferred Share is equivalent to such number of Ordinary Shares as is converted in accordance with the Conversion Rate and, if applicable, adjusted in accordance with Article 8.8;
Associate	in relation to any person means any person who is an associate of that person and the question of whether a person is an associate of another is to be determined in accordance with section 435 of the Insolvency Act 1986 and (whether or not an associate as so determined): (a) any Member of the Same Group; and (b) any Member of the Same Fund Group;
Atlas	Atlas Venture Fund VIII, L.P. of 25 First Street, Suite 303, Cambridge MA 02141;
Auditors	the auditors of the Company from time to time;
Available Profits	profits available for distribution within the meaning of section 830 of the 2006 Act;
B Ordinary Conversion Rate	the conversion rate of one B Ordinary Share into one Ordinary Share, subject to adjustment in accordance with Article 8.8;

B Ordinary Issue Price	the B1 Ordinary Issue Price or the B2 Ordinary Issue Price (as applicable);
B Ordinary Shares	the B1 Ordinary Shares and the B2 Ordinary Shares;
B Ordinary Shareholders	the B1 Ordinary Shareholders and the B2 Ordinary Shareholders;
B1 Ordinary Conversion Rate	the conversion rate of one B1 Ordinary Share into one Ordinary Share, subject to adjustment in accordance with Article 8.8;
B1 Ordinary Issue Price	in respect of each B1 Ordinary Share: (a) in issue prior to the Date of Adoption and held by an Investor (save for Ahren), £11.2278 per Ordinary Share; (b) in issue prior to the Date of Adoption held by Ahren, £13 per Ordinary Share; and (c) issued on or after the Date of Adoption, the price at which the relevant B1 Ordinary Share is issued including any premium, subject to the appropriate proportionate adjustment following any Capital Reorganisation;
B1 Ordinary Shares	the B1 ordinary shares of £0.01 each in the capital of the Company;
B1 Ordinary Shareholders	the holders of the B1 Ordinary Shares;
B2 Ordinary Conversion Rate	the conversion rate of one B2 Ordinary Share into one Ordinary Share, subject to adjustment in accordance with Article 8.8;
B2 Ordinary Issue Price	in respect of each B2 Ordinary Share: (a) issued on the Date of Adoption, £15.55 per B2 Ordinary Share; and (b) issued after the Date of Adoption, the price at which the relevant B2 Ordinary Share is issued including any premium, subject to the appropriate proportionate adjustment following any Capital Reorganisation;
B2 Ordinary Shares	the B2 ordinary shares of £0.01 each in the capital of the Company;
B2 Ordinary Shareholders	the holders of the B2 Ordinary Shares;
Bad Leaver	an Employee whose employment or consultancy is terminated by a Group Company either in circumstances which justify summary dismissal under the relevant service contract or as a result of the breach by the Employee of any Restrictive Covenants in such Employee's employment or consultancy agreement or any Former Employee who breaches any Restrictive Covenants in such Former Employee's employment or consultancy agreement
Bad Leaver Date	shall have the meaning given to the term in Article 15.5;
Board	the board of Directors and any committee of the board constituted for the purpose of taking any action or decision contemplated by these Articles;
Bona Fide Offer	an offer made in writing by a bona fide arm's length purchaser to acquire a specified number of Shares (and/or assets) and which indicates: (i) the type, number and class of Shares (and/or assets) to be purchased, (ii) the price offered, (iii) the other material terms and conditions of the offer, and (iv) the name and address of the offeror and of each person who controls it, provided that such offer may not be subject to any conditions the

satisfaction or fulfilment of which is within the control of such third party;

Bonus Shares shall have the meaning given to the term in Article 5.6;

Business Day a day on which English clearing banks are ordinarily open for the transaction of normal banking business in the City of London (other than a Saturday or Sunday);

Business Sale (a) a Subsidiary Share Sale; or (b) the disposition of all or substantially all of the assets or businesses of the Company to a third party (either by way of a sale, licence and/or other transfer), save where any such disposition is effected solely for the purpose of a disposition or demerger of the assets of any Group Company (in whole or in part) to a newly incorporated company which will be owned (as applicable) by the Company or the Shareholders (and if by the Shareholders, in the same proportions and on the same terms as they hold the Shares);

Buyback Agreement shall have the meaning given to the term in Article 15.6;

Capital Reorganisation shall mean any of the following:

(a) issue of Shares fully or partly paid up pursuant to a capitalisation of profits or reserves (including any share premium account or capital redemption reserve) but excluding any Permitted Capitalisation Issue and any Shares that are required to be issued pursuant to any agreement among the Company and Shareholders constituting a Super Preferred Majority;

(b) sub-division or consolidation of Shares;

(c) reduction of capital, or other reduction in the number of Shares in issue from time to time;

(d) redesignation or re-classification of any shares in the capital of the Company;

(e) the redemption or repurchase of any shares in the capital of the Company; or

(f) any other reorganisation of the share capital of the Company,

save where any of the above is effected solely for the purpose of a demerger of the assets of any Group Company (in whole or in part) to a newly incorporated company which will be owned by the Shareholders (in the same proportions, disregarding any Shares held by the Company, as they hold Shares);

CIC Cambridge Innovation Capital (Jersey) Limited (company number 112629) whose registered office is at Gaspé House, 66-72 Esplanade, St Helier, Jersey, JE2 3QT and its Permitted Transferees;

CIC Director the Director appointed by CIC and/or its Permitted Transferees pursuant to Article 25.6;

CIC Investors (i) the CIC Group Companies; and (ii) any company, body corporate, partnership, limited partnership, limited liability partnership, unincorporated association, fund, unit trust, collective investment undertaking, collective investment scheme, co-investment scheme, separate managed account, pooled investment vehicle, investment holding vehicle, parallel vehicle (however configured) of which a CIC Group Company is (a) the investment manager (or an authorised representative of the investment manager) or (b) an investment adviser (or an authorised representative of the investment adviser) or (c) an operator or (d) the general partner or (e) a managing

	member; and (iii) trustee, nominee or custodian of any of the foregoing;
CIC Group Companies	CIC plc, any company that becomes a Parent Undertaking of CIC plc and the shareholders of which are, at the time of so becoming, substantially the same as the shareholders in CIC plc immediately prior to such time (**CIC HoldCo**), and each of their respective Subsidiary Undertakings from time to time that are investment vehicles for funds raised by CIC plc or a CIC HoldCo;
CIC Group Representative	whichever of the CIC Group Companies is designated by CIC plc in writing to the Company as the "CIC Group Representative" from time to time;
CIC plc	Cambridge Innovation Capital plc (Company No 08243718) whose registered office is at Hauser Forum, 3 Charles Babbage Road, Cambridge CB3 OGT;
Civil Partner	in relation to a Shareholder, a civil partner (as defined in the Civil Partnerships Act 2004) of the Shareholder;
Commencement Date	the date the relevant Employee first commences his employment or consultancy with any Group Company;
Company	Bicycle Therapeutics Limited (company no. 11036004);
Compulsory Transfer	means any transfer of a Share required under Article 15;
Conditions	shall have the meaning given to the term in Article 8.1;
Controlling Interest	an interest in shares giving to the holder or holders control of the Company within the meaning of section 1124 of the Corporation Tax Act 2010;
Conversion Date	shall have the meaning given to the term in Article 8.1;
Conversion Rate	the A Ordinary Conversion Rate or the B Ordinary Conversion Rate (as applicable);
Date of Adoption	the date on which these Articles were adopted;
Delayed Consideration	shall have the meaning given to the term in Article 5.10;
Director(s)	a director or directors of the Company from time to time;
Effective Termination Date	the date on which the Employee's employment or consultancy or office with the relevant Group Company terminates;
Employee	an individual who is employed by, seconded to or who provides consultancy services to a Group Company and any Director of any Group Company (excluding Sir Gregory Winter);
Employee Share Plan(s)	the Employee share option or share purchase plan(s) of the Company, the terms of which have been approved by the Investor Directors;
Employee Shares	in relation to an Employee or Former Employee means all Ordinary Shares held by: (a) the Employee or Former Employee in question; and (b) by any Permitted Transferee of that Employee or Former Employee other than those Ordinary Shares held by those persons that a Preferred Majority is satisfied were not acquired directly or indirectly from the Employee or Former Employee or by reason of his/her relationship with the Employee or Former Employee;
Employee Trust	a trust, the terms of which are approved by a Preferred Majority, whose

beneficiaries are the Employees;

Entitlement Amount shall have the meaning given to the term in Article 5.10;

Exempt Issuances shall mean:

(a) Ordinary Shares issued to Employees under any Employee Share Plan or options to subscribe for Ordinary Shares under any Employee Share Plan;

(b) any Shares or securities issued or granted in order for the Company to comply with its obligations under Articles 5.6, 5.8 and 8.7;

(c) any Shares or securities issued in consideration of the acquisition by the Company of any company or business which has been approved in writing by a Preferred Majority;

(d) any Shares or securities which a Preferred Majority has agreed in writing should be issued without complying with the procedure set out in Article 10;

(e) any Shares or securities issued to all Shareholders, pro rata to their existing holdings of Ordinary Shares on an As Converted Basis as a result of a bonus issue of shares which has been approved in writing by a Preferred Majority;

(f) any Shares issued pursuant to the exercise of any Warrant granted by the Company on or before the Date of Adoption;

(g) any shares issued pursuant to a Holding Company Reorganisation;

(h) any Shares or securities issued in connection with a strategic transaction approved by a Preferred Majority; and

(i) any Shares or securities issued on an IPO;

Family Trusts as regards any particular individual member or deceased or former individual member, trusts (whether arising under a settlement, declaration of trust or other instrument by whomsoever or wheresoever made or under a testamentary disposition or on an intestacy) under which no immediate beneficial interest in any of the shares in question is for the time being vested in any person other than the individual and/or Privileged Relations of that individual; and so that for this purpose a person shall be considered to be beneficially interested in a share if such share or the income thereof is liable to be transferred or paid or applied or appointed to or for the benefit of such person or any voting or other rights attaching thereto are exercisable by or as directed by such person pursuant to the terms of the relevant trusts or in consequence of an exercise of a power or discretion conferred thereby on any person or persons;

Financial Institution any financial investor registered with the Financial Conduct Authority (or a financial investor registered with the equivalent body or authority in the

country of the relevant financial investor's principal place of business);

Financial Year and Financial Period	an accounting reference period (as defined by the 2006 Act) of the Company;
Former Employee	an Employee whose employment or consultancy or office with any Group Company has terminated;
Founders	Sir Gregory Winter and Dr. Christian Heinis and each a "**Founder**";
Founder Director	Sir Gregory Winter or such other director appointed to replace him from time to time;
Fund Manager	a person whose principal business is to make, manage or advise upon investments in securities;
Group	the Company, its Parent Undertaking(s) (if any) and its Subsidiary Undertaking(s) (if any) and any Subsidiary Undertaking(s) of any such Parent Undertaking, from time to time, and "**Group Company**" shall be construed accordingly;
Holding Company	means a holding company of the Company newly incorporated in any jurisdiction (including, without limitation, in the United States under Delaware law) which has no previous trading history and has resulted from a Holding Company Reorganisation;
Holding Company Reorganisation	means any transaction involving the issue of shares in the capital of a Holding Company to the Shareholders, the object or intent of which is to interpose the Holding Company as the sole owner of the Company prior to an IPO such that immediately subsequent to such transaction: a) the number and class of shares comprised in the issued share capital of the Holding Company, the identity of the shareholders of the Holding Company, and the number and class of shares held by each such person is the same as the issued share capital of the Company and the identity of Shareholders and the number and class of Shares held by each such person immediately prior to such transaction (save for the fact that such shares are issued by a different company); b) the rights attaching to each class of share comprised in the Holding Company are the same as those rights attaching to the like class of share comprised in the share capital of the Company immediately prior to such transaction (save for the fact that such shares are issued by a different company and/or in a different jurisdiction with attendant differences in company law); and c) the constitutional documents of the Holding Company are the same in effect as the articles of association of the Company immediately prior to such acquisition (save for the fact that they apply in respect of a different company, and as to matters and modifications to reflect that the Holding Company may be incorporated in a jurisdiction other than England and Wales);
Independent Director	any Director of the Company appointed pursuant to Article 25.10;
Initial Consideration	shall have the meaning given to the term in Article 5.10;
Institutional Investor	a fund, partnership, body corporate, trust or other person or entity whose principal business is to make investments or a person whose business is to

	make, manage or advise upon investments for any of the foregoing;
Investor Director	any Director of the Company appointed pursuant to Articles 25.1 to 25.7;
Investor Director Consent	the prior written consent of a majority of Investor Directors appointed from time to time;
IPO	the admission of (or in the case of admission to Nasdaq, the closing of the initial public offering of) all or any of the Shares or securities representing those shares (including without limitation American depositary receipts, American depositary shares and/or other instruments) on Nasdaq or on the Official List of the United Kingdom Listing Authority or on the AIM Market operated by the London Stock Exchange Plc or any other recognised investment exchange (as defined in section 285 of the Financial Services and Markets Act 2000);
Issue Price	shall mean the A Ordinary Issue Price or the B Ordinary Issue Price (as applicable);
ITEPA	Income Tax (Earnings and Pensions) Act 2003;
Leaver's Percentage	in relation to and for the purposes of determining the number of Employee Shares that are required (pursuant to Article 15.5) to be compulsorily transferred to the Company as a result of an Employee ceasing to be an Employee, the percentage (rounded up to two decimal places), shall be: (a) in accordance with the applicable vesting schedule set out in any Share Subscription Agreement or employment or consultancy agreement entered into between the Employee and any Group Company such that the Leaver's Percentage shall constitute any unvested shares pursuant to the applicable agreement on the Effective Termination Date, provided that if an Employee is a Bad Leaver, the Leaver's Percentage of any Employee Shares shall be 100% of the Employee Shares held by such Employee on the Effective Termination Date, and (b) in respect of Employees whose shares are not subject to further vesting, including Shares acquired upon exercise of options granted under any Employee Share Plan, and Former Employees who in each case are Bad Leavers, either 100% of the Employee Shares held by such Employee on the Effective Termination Date or 100% of the Employee Shares held by such Former Employee at the time of the breach of such Former Employee's Restrictive Covenants (as the case may be);
Liquidation Event or Liquidation	shall mean any of the following events: (a) the liquidation or winding up of the Company; or (b) dissolution of the Company for reasons other than those falling under the definition of Sale;
Longwood	Longwood Fund IV, L.P. of 800 Boylston Suite 1555, Boston, Massachusetts, 02199, USA;
a Member of the Same Fund Group	if the Shareholder is a fund, partnership, company, syndicate or other entity whose business is managed by a Fund Manager (an "**Investment Fund**") or a nominee of that Investment Fund or Fund Manager: (a) any participant or partner in or member of any such Investment Fund or the holders of any unit trust which is a

	participant or partner in or member of any Investment Fund; (b) any fund managed or advised by such Investment Fund's Fund Manager; or (c) any Parent Undertaking or Subsidiary Undertaking of such Fund Manager, or any Subsidiary Undertaking of any Parent Undertaking of such Fund Manager; or (d) any trustee, nominee or custodian of such Investment Fund and vice versa;
a Member of the Same Group	as regards any company, a company which is from time to time a Parent Undertaking or a Subsidiary Undertaking of that company or a Subsidiary Undertaking of any such Parent Undertaking;
Minor Sale	the disposition of any asset(s) or any business(es) of the Company to a third party (either by way of a sale, licence and/or other transfer) which would not otherwise constitute a Business Sale;
Minor Sale Proceeds	shall have the meaning given to the term in Article 5.4(b);
Nasdaq	the Nasdaq National Stock Market of the Nasdaq Stock Market Inc.;
New Securities	any shares (or other securities convertible into, or carrying the right to subscribe for, shares) issued by the Company after the Date of Adoption other than Exempt Issuances;
Non-Cash Consideration	shall have the meaning given to the term in Article 5.9;
Novartis	Novartis Bioventures Ltd. of Lichtstrasse 35, 4056 Basel, Switzerland;
Ordinary Shareholders	the holders from time to time of the Ordinary Shares;
Ordinary Shares	the ordinary shares of £0.01 each in the capital of the Company;
Original Shareholder	shall have the meaning given to the term in Article 13.1;
Permitted Capitalisation	an issue of Shares by the Company credited as fully paid up as to nominal value from any share premium account of the Company

Issue	(or otherwise lawfully paid up from a capitalisation of profits or reserves (including any capital redemption reserve)) made pursuant to Article 5;
Permitted Transfer	a transfer of Shares in accordance with Article 13;
Permitted Transferee	shall mean any of the following: (a) in relation to a Shareholder who is an individual, any of his Privileged Relations or Trustees; (b) in relation to a Shareholder which is an undertaking (as defined in section 1161 of the 2006 Act), any Member of the Same Group; (c) in relation to a Shareholder which is an Investment Fund, any Member of the Same Fund Group; (d) in relation to a Preferred Shareholder: i. to any Member of the Same Group; ii. to any Member of the Same Fund Group; iii. subject to Investor Director Consent, to any other Preferred

Shareholder;

iv. subject to Investor Director Consent, to any Financial Institution or Institutional Investor;

v. to any bare nominee of such Preferred Shareholder; or

vi. subject to Investor Director Consent, to any general or limited partners of a Preferred Shareholder or to shareholders operating as a limited partnership or similar;

(e) in relation to UKRI, any successor body of UKRI which takes over all or substantially all of the business and functions of UKRI;

(f) in relation to EPFL, any entity which is controlled by EPFL and which takes over EPFL activities in connection with equity holdings management; and

(g) in relation to CIC or a CIC Investor:

vii. to any Member of the same Group;

viii. to any Member of the same Fund Group; and

ix. any other CIC Investor;

Preferred Majority	the Preferred Shareholders holding more than fifty percent (50%) of the number of Ordinary Shares held by Preferred Shareholders on an As Converted Basis;
Preferred Shareholders	the B Ordinary Shareholders and/or the A Ordinary Shareholders as the context requires;
Preferred Shares	the B Ordinary Shares and/or the A Ordinary Shares as the context requires;
Priority Rights	the rights of Shareholders to purchase Shares contained in a Transfer Notice in the priority stipulated in Article 14.6;
Privileged Relation	in relation to a Shareholder who is an individual member or deceased or former member means a spouse, Civil Partner, child or grandchild (including step or adopted or illegitimate child and their issue);
Proceeds	shall have the meaning given to the term in Article 5.6;
Proceeds of Sale	the consideration payable (including any deferred consideration) whether in cash or otherwise to those Shareholders selling Shares under a Share Sale or to the Company selling shares in any Subsidiary under a Subsidiary Share Sale, in each case net of any transaction costs;
Proposed Exit	shall have the meaning given to the term in Article 6.2;
Proposed Purchaser	a proposed purchaser who at the relevant time has made an offer on arm's length terms;
Proposed Seller	any person proposing to transfer any shares in the capital of the Company;
Qualified IPO	the admission of (or in the case of admission to Nasdaq, the closing of the initial public offering of) all the Shares or securities representing those shares (including without limitation American depositary receipts, American depositary shares and/or other instruments) on Nasdaq, or on the Official List of the United Kingdom Listing Authority, the AIM Market or any other recognised investment exchange at a per share public offering price of not less than two times the B2 Ordinary Issue Price (as at the date of Adoption)

	for a total offering size of not less than £50 million;
Qualifying Company	shall have the meaning given to the term in Article 13.7;
Qualifying Issue	shall have the meaning given to the term in Article 8.8;
Restrictive Covenants	obligations in respect of confidentiality, intellectual property, non-solicitation, non-dealing, non-poaching and/or non-competition;
Restricted Member	shall have the meaning given to the term in Article 15.8;
Sale Shares	shall have the meaning given to the term in Article 14.2(a);
Sale or Sale Event	shall mean any of the following: (a) a Business Sale, unless deemed not to be a Sale Event by a Preferred Majority; or (b) a Share Sale, (each of the foregoing being referred to individually as a "**Sale Event**");
Seller	shall have the meaning given to the term in Article 14.2;
Shareholder	any holder of any Shares;
Shares	the Ordinary Shares, the A Ordinary Shares and B Ordinary Shares from time to time;
Share Sale	a sale or other transfer of the whole or any part of the issued share capital of the Company on arm's length terms to any person (or any merger or scheme of arrangement resulting in any persons holding Shares) and resulting in that person together with all persons (if any) acting in concert (within the meaning given in the City Code on Takeovers and Mergers) with such person together holding a Controlling Interest in the Company;
Share Subscription Agreement	any agreement between the Company and an Employee relating to the subscription and vesting of the Employee Shares;
S.R. One	S.R. One, Limited of Corporation Service Company, 2595 Interstate Drive, Suite 103, Harrisburg, PA 17110, USA;
Subsidiary, Subsidiary Undertaking and Parent Undertaking	shall have the meanings given to the terms in the 2006 Act;
Subsidiary Share Sale	a sale or other transfer of the whole or any part of the issued share capital of a Subsidiary by the Company on arm's length terms to any person which is not a member of the Group (or any merger or scheme of arrangement resulting in any such persons holding shares) and resulting in that person together with all persons (if any) acting in concert (within the meaning given in the City Code on Takeovers and Mergers) with such person together holding a Controlling Interest in the Subsidiary;
Super Preferred Majority	the Preferred Shareholders holding more than seventy seven percent (77%) of the number of Ordinary Shares held by Preferred Shareholders on an As Converted Basis;
Surplus Assets	the surplus assets of the Company remaining after the payment (or other satisfaction) of its liabilities;
SVLSA	SV Life Sciences Fund V Strategic Partners, L.P. and/or SV Life Sciences

	Fund V, L.P. of One Boston Place, Suite 3900, Boston, MA 02118 USA;
Trust Account	shall have the meaning given to the term in Article 5.11;
Transfer Notice	shall have the meaning given to the term in Article 15.5;
Transfer Price	shall have the meaning given to the term in Article 14.2(c);
Trustees	in relation to a Shareholder means the trustee or the trustees of a Family Trust;
Tybourne	Aquila Investments IV, a limited liability company incorporated under the laws of the Cayman Islands with company number 320149 whose registered office is at Maples Corporate Services Limited, PO Box 309, Ugland House, Grand Cayman, KY1-1104 Cayman Islands;
UKRI	United Kingdom Research and Innovation of Polaris House, North Star Avenue, Swindon, SW2;
Vertex	Vertex Global HC Fund I Pte. Ltd. of 250 North Bridge Road, #11-01 Raffles City Tower, Singapore 179101; and
Warrants	the warrants to subscribe for A Ordinary Shares or B1 Ordinary Shares granted by the Company on or prior to the date of Adoption pursuant to any warrant instrument (as may be amended from time to time in accordance with its terms) entered into by the Company.

3. SHARE CAPITAL

3.1 In these Articles, unless the context requires otherwise, references to shares of a particular class shall include shares created and/or issued on or after the Date of Adoption and ranking pari passu in all respects (or in all respects except only as to the date from which those shares rank for dividend) with the shares of the relevant class then in issue.

3.2 Except as otherwise provided in these Articles, the B2 Ordinary Shares, the B1 Ordinary Shares, the A Ordinary Shares and the Ordinary Shares shall rank pari passu in all respects but shall constitute separate classes of shares.

4. DIVIDENDS

4.1 In respect of any Financial Year, the Available Profits of the Company will be applied as set out in this Article 4.

4.2 The Preferred Shares shall rank pari passu in all respects as to dividends with the Ordinary Shares on an As Converted Basis. No dividend shall be declared or paid on the Ordinary Shares without a like dividend being declared or paid, as the case may be, on the Preferred Shares on an As Converted Basis.

4.3 Every dividend shall be distributed to the appropriate shareholders pro rata according to the numbers of shares held by them respectively and shall accrue on a daily basis assuming a 365 day year. All dividends are expressed net and shall be paid in cash.

4.4 If the Company is unable to pay in full on the due date any dividend by reason of having insufficient Available Profits then it will on that date pay it to the extent that it is then lawfully able to do so.

4.5 The Company will procure that the profits of any other Group Company available for distribution will be paid by way of dividend to the Company (or, as the case may be, the relevant Group Company that is its immediate holding company or Parent Undertaking) if and to the extent that dividends are necessary to permit lawful and prompt payment by the Company of the shareholder dividends.

4.6 Subject to the 2006 Act, these Articles and Investor Director Consent, the Board may pay interim dividends if justified by the Available Profits in respect of the relevant period.

5. DISTRIBUTIONS FOLLOWING A LIQUIDATION OR SALE EVENT

5.1 On a Liquidation or Sale Event, the Surplus Assets (in the case of a Liquidation or a Business Sale which is not a Subsidiary Share Sale) or the Proceeds of Sale (in the case of a Share Sale or a Subsidiary Share Sale) shall be applied amongst, and distributed to, the Shareholders in the following order of priority (to the extent that the Company is lawfully permitted to do so):

(a) first in paying to each of the B2 Ordinary Shareholders, in priority to any other classes of Shares, an amount per B2 Ordinary Share held equal to the B2 Ordinary Issue Price plus accrued and unpaid dividends (provided that if there are insufficient Surplus Assets or Proceeds of Sale (as applicable) to pay the amounts required, the remaining Surplus Assets or Proceeds of Sale (as applicable) shall be distributed to the B2 Ordinary Shareholders pro rata to the aggregate B2 Ordinary Issue Price applicable to their respective holdings of B2 Ordinary Shares;

(b) second in paying to each of the B1 Ordinary Shareholders, in priority to the A Ordinary Shares, an amount per B1 Ordinary Share held equal to the B1 Ordinary Issue Price plus accrued and unpaid dividends (provided that if there are insufficient Surplus Assets or Proceeds of Sale (as applicable) to pay the amounts required, the remaining Surplus Assets or Proceeds of Sale (as applicable) shall be distributed to the B1 Ordinary Shareholders pro rata to the aggregate B1 Ordinary Issue Price applicable to their respective holdings of B1 Ordinary Shares);

(c) third in paying to each of the A Ordinary Shareholders, in priority to the Ordinary Shares, an amount per A Ordinary Share held equal to the A Ordinary Issue Price plus accrued and unpaid dividends (provided that if there are insufficient Surplus Assets or Proceeds of Sale (as applicable) to pay the amounts required, the remaining Surplus Assets or Proceeds of Sale (as applicable) shall be distributed to the A Ordinary Shareholders pro rata to the aggregate A Ordinary Issue Price applicable to their respective holdings of A Ordinary Shares); and

(d) the balance of the Surplus Assets or the Proceeds of Sale (as applicable) (if any) shall be distributed among the holders of Shares pro rata on an As Converted Basis (as if the Shares constituted one and the same class) to the number of Shares held.

5.2 Article 5.3 applies if:

(a) the exercise period for any Warrants has commenced but not expired; and

(b) any rights to exercise such Warrants remain exercisable but unexercised and the Warrants remain exercisable immediately before the application of Article 5.1 in accordance with the terms of any such Warrants.

5.3 If this Articles 5.3 applies, each holder of such Warrants shall, for the purposes of ascertaining its rights under Article 5.1, be treated as if it had, immediately before the application of Article 5.1, fully exercised its outstanding rights to exercise such Warrants and subscribe for the relevant Shares, after deducting a sum equal to the subscription price that would have been payable for the relevant Shares (but nothing in this Article 5.3 shall require a holder of Warrants to make any payment to the Company or any other person).

5.4 As soon as practicable after the receipt of consideration payable to the Company in respect of:

(a) a Business Sale; or

(b) a Minor Sale, following which the Board has determined that the relevant proceeds are to be distributed to Shareholders ("**Minor Sale Proceeds**"),

the Company shall distribute the Surplus Assets, the Proceeds of Sale from a Subsidiary Share Sale or the Minor Sale Proceeds, as applicable, to the Shareholders by means of a dividend or other distribution in accordance with the order of priorities set out in Article 5.1. For the purposes of effecting such distribution, the Board shall have authority to procure the liquidation of the Company or to distribute the Surplus Assets, the Proceeds of Sale from a Subsidiary Share Sale or the Minor Sale Proceeds to the Shareholders by way of dividend or otherwise. The provisions of this Article shall prevail over all other provisions of these Articles.

5.5 The total amount of the applicable Issue Price payable to the B Ordinary Shareholders (pursuant to Article 5.1(a) and Article 5.1(b)) and the A Ordinary Shareholders (pursuant to Article 5.1(c)) shall be payable once, however such amounts may be satisfied in any number of payments. Accordingly, if distributions are made pursuant to Article 5.1 on more than one occasion, each such distribution shall take into account all previous distributions made pursuant to Article 5.1, on a cumulative basis.

5.6 On an IPO other than a Qualified IPO, the Company shall issue to each holder for the time being of Preferred Shares, such number (if any) of Ordinary Shares (the "**Bonus Shares**") so that the proportion of the Ordinary Shares held by that Preferred Shareholder on an As Converted Basis (following the issue of such Ordinary Shares) as against the total issued share capital of the Company, equals the proportion of the proceeds that such Preferred Shareholder would have been entitled to receive on a Liquidation or Sale Event pursuant to Article 5.1 (the "**Proceeds**"). For the purposes of this Article, the Proceeds shall be calculated by multiplying the total number of Ordinary Shares in issue immediately after the IPO (but excluding the Bonus Shares issued pursuant to this Article and any shares issued in return for new monies raised pursuant to such IPO) by the price per Ordinary Share issued by the Company pursuant to such IPO.

5.7 The Bonus Shares issued pursuant to Article 5.6 shall be paid up by the automatic capitalisation of any amount standing to the credit of the share premium account or any other available reserve of the Company as determined by the Directors, and such Bonus Shares shall be issued at their nominal value fully paid. Such capitalisation shall not require any action on the part of the Shareholders, and the Directors shall allot the Bonus Shares arising on such capitalisation to the Preferred Shareholders in accordance with this Article. To the extent that there is insufficient share capital to effect the said issue, the Directors shall procure (so far as they are able) that the Company's share capital is increased to the extent necessary to permit the issue required and all Shareholders shall vote in favour of the necessary resolutions to effect such increase.

5.8 To the extent that there are insufficient distributable reserves to effect the issue of Bonus Shares as set out above, such issue of Bonus Shares shall be subscribed for by the Preferred Shareholders paid up to their nominal value.

5.9 If the Surplus Assets, the Proceeds of Sale or the Minor Sale Proceeds include any non-cash consideration (the "**Non-Cash Consideration**") then, for the purposes of Articles 5.1 and 5.4 such Non-Cash Consideration shall be deemed to have a cash value equal to such amount as the Auditors (acting as experts and not as arbitrators) may, at the cost of the Company, determine (in their opinion) represents a reasonable estimation of the market value of such Non-Cash Consideration as at the date of such Business Sale, Minor Sale or Share Sale (as the case may be), taking into account such matters, facts and circumstances as the Auditors (in their sole discretion) consider reasonable. In the absence of fraud or manifest error, such determination of the Auditors shall be final and binding on all Shareholders.

5.10 If the Surplus Assets or Proceeds of Sale or Minor Sale Proceeds include any deferred and/or contingent consideration, including any consideration held in an escrow account for the purpose of satisfying claims by the buyer in connection with a Business Sale or a Share Sale or a Minor Sale, (the "**Delayed Consideration**") (and after having determined the deemed

value of such Delayed Consideration in accordance with Article 5.9 if such consideration is also Non-Cash Consideration) then for the purposes of Articles 5.1 and 5.4, the potential value of any Delayed Consideration shall be excluded for the purposes of calculating any initial distribution to be made in consequence of such Business Sale or Share Sale or Minor Sale (as the case may be) and only such of the Surplus Assets or Proceeds of Sale or Minor Sale Proceeds which are not Delayed Consideration (the "**Initial Consideration**") shall then be distributed in accordance with Articles 5.1 and 5.4. Subsequent distributions pursuant to Articles 5.1 and 5.4 shall be made as Surplus Assets or Proceeds of Sale or Minor Sale Proceeds become available and as at the time of each distribution of the Delayed Consideration the entitlement of each Shareholder in accordance with Articles 5.1 and 5.4 (including the amounts previously distributed plus the Delayed Consideration to be then distributed) (the "**Entitlement Amount**") shall be recalculated and distributed so as to make good any shortfall between the Initial Consideration previously distributed and the Entitlement Amount of each Shareholder. Notwithstanding the foregoing provisions, no Shareholder shall be required to repay or otherwise relinquish any amount previously distributed to them (unless expressly agreed by such Shareholder) in the event that its Entitlement Amount as so calculated is less than the amount of any prior distribution of Surplus Assets or Proceeds of Sale or Minor Sale Proceeds actually made to it under Articles 5.1 and 5.4.

5.11 In the event of a Share Sale then, notwithstanding anything to the contrary in the terms and conditions governing such Share Sale or otherwise, the Company may (and shall, if required to do so by a Preferred Majority) establish a designated trust account in the name of such person as the Company (with the approval of a Preferred Majority) may determine to be a suitable person to act as trustee (the "**Trust Account**"). The Proceeds of Sale shall be paid into such Trust Account and thereafter distributed in accordance with the order of priority set out in Article 5.1 (subject to the further provisions of Articles 5.5 to 5.10) and each Shareholder shall be bound, and is hereby deemed, to direct that his entitlement shall be paid into the Trust Account pending distribution in accordance with Article 5.1.

5.12 Regulation 117 of Table A shall be subject to the provisions of this Article 5;

6. SALE PROVISIONS

6.1 On a Sale Event, the Directors shall not register any transfer of Shares if the Proceeds of Sale are not distributed in accordance with Article 5 save in respect of any Shares not sold in connection with that Sale Event, provided that if the Proceeds of Sale are not settled in their entirety upon completion of the Sale Event:

(a) the Directors shall not be prohibited from registering the transfer of the relevant Shares so long as the Proceeds of Sale that are settled have been distributed in the order of priority set out in Article 5; and

(b) the Shareholders shall take any action required by a Preferred Majority to ensure that the Proceeds of Sale in their entirety are distributed in the order of priority set out in Article 5.

6.2 Upon the occurrence of a Sale Event approved by the Board and approved under these Articles or following the approval of a Super Preferred Majority (the "**Proposed Exit**"), each Shareholder shall consent to, vote for, raise no objections to and waive any applicable rights (except any rights expressly provided for in these Articles or any agreement between the Company that Shareholder) in connection with the Proposed Exit (the "**Actions**"). The Shareholders shall be required to take all Actions with respect to the Proposed Exit as are reasonably required by the Board to facilitate the Proposed Exit. If any Shareholder fails to comply with the provisions of this Article, the Company shall be constituted the agent of each defaulting Shareholder for taking such Actions as are necessary to effect the Proposed Exit and the Directors may authorise an officer or member to execute and deliver on behalf of such defaulting Shareholder the necessary documents and the Company may receive any purchase money due to the defaulting Shareholder on trust for each of the defaulting

Shareholders. Notwithstanding the provisions of this Article 6.2, no Preferred Shareholder may be required in connection with any Proposed Exit to:

(a) enter into any undertakings or covenants (including any non-competition, non-solicitation, no-hire or any other restrictive covenants);

(b) give any representations or warranties, or provide any indemnities, save for representations or warranties (to be given severally, and not jointly or jointly and severally) in respect of the following:

(i) that such Preferred Shareholder has the authority to transfer its Shares, is the legal and beneficial owner of its Shares and has good and valid title to its Shares, free and clear of any and all encumbrances; or

(ii) to the extent securities are offered, in whole or in part, as consideration to such Preferred Shareholder, such customary warranties and/or representations as may be required under any applicable laws or by any applicable regulatory authority so as to ensure that those securities may lawfully be offered and issued to the Preferred Shareholder.

7. VOTES IN GENERAL MEETING

7.1 The B Ordinary Shares shall confer on each B Ordinary Shareholder the right to receive notice of and to attend, speak and vote at all general meetings of the Company.

7.2 The A Ordinary Shares shall confer on each A Ordinary Shareholder the right to receive notice of and to attend, speak and vote at all general meetings of the Company.

7.3 The Ordinary Shares shall confer on each Ordinary Shareholder the right to receive notice of and to attend, speak and vote at all general meetings of the Company.

7.4 Where the Shares confer a right to vote, on a show of hands each Shareholder who (being an individual) is present in person or by proxy or (being a corporation) is present by a duly authorised representative or by proxy shall have one (1) vote and on a poll each such Shareholder so present shall have:

(a) one (1) vote for each Ordinary Share held by him; and

(b) in the case of any Preferred Shareholder, one (1) vote per Ordinary Share such Preferred Shareholder would hold on an As Converted Basis.

7.5 The Preferred Shareholders will vote together with the Ordinary Shareholders and not as a separate class except as specifically provided herein or otherwise required by law.

8. CONVERSION OF PREFERRED SHARES

8.1 Each Preferred Shareholder shall be entitled, by notice in writing to the Company, to require conversion into Ordinary Shares of all of the Preferred Shares held by it at the Conversion Rate at any time and those Preferred Shares shall convert at the Conversion Rate into Ordinary Shares automatically on the date the Preferred Shareholder (the "**Conversion Date**") gives such notice. The holder may in such notice, state that conversion of its Preferred Shares into Ordinary Shares is conditional upon the occurrence of particular events (the "**Conditions**").

8.2 All of the Preferred Shares shall automatically convert at the Conversion Rate into Ordinary Shares immediately:

(a) prior to occurrence of a Qualified IPO; and

(b) at the election of a Super Preferred Majority.

8.3 In the case of:

(a) Article 8.1, no later than five (5) Business Days after the Conversion Date;

(b) Article 8.2(a), at least five (5) Business Days prior to the occurrence of the Qualified IPO; and

(c) Article 8.2(b), no later than five (5) Business Days following the election of a Super Preferred Majority,

each Preferred Shareholder shall deliver the certificate (or an indemnity in a form reasonably satisfactory to the Board in respect of any lost certificate(s)) in respect of the Preferred Shares being converted to the Company at its registered office at that time.

8.4 Where conversion is mandatory on the occurrence of a Qualified IPO, that conversion will be effective only immediately prior to such Qualified IPO (and Conversion Date shall be construed accordingly) and if such Qualified IPO does not become effective or does not take place, such conversion shall be deemed not to have occurred. In the event of a conversion under Article 8.1, if the Conditions have not been satisfied or waived by the relevant Shareholder by the Conversion Date such conversion shall be deemed not to have occurred.

8.5 Subject to Article 8.7, on the Conversion Date, the relevant Preferred Shares shall without further authority than is contained in these Articles stand converted into Ordinary Shares at the relevant Conversion Rate and the Ordinary Shares resulting from that conversion shall in all other respects rank pari passu with the existing issued Ordinary Shares.

8.6 Subject to Article 8.7, the Company shall on the Conversion Date enter the Preferred Shareholder into the register of members of the Company as the holder of the appropriate number of Ordinary Shares and, subject to the relevant holder delivering its certificate(s) (or indemnity) in respect of the Preferred Shares it held in accordance with this Article 8, the Company shall within ten (10) Business Days of the Conversion Date forward to such Preferred Shareholder by post to his address shown in the register of members, free of charge, a definitive certificate for the appropriate number of fully paid Ordinary Shares.

8.7 If the number of Ordinary Shares resulting from the conversion of any Preferred Shares held by a Preferred Shareholder is greater than the number of the Preferred Shares being converted, the Company shall issue to the Preferred Shareholder such number of Ordinary Shares (fully paid as to their nominal value) as is equal to the excess. To the extent that the Company lacks, and is unable lawfully to create, sufficient distributable reserves to effect such an issue of fully paid Ordinary Shares, the Preferred Shareholder shall be entitled to subscribe for the relevant Ordinary Shares at nominal value together with such additional number of Ordinary Shares (at nominal value) as is necessary to compensate that Preferred Shareholder for the subscription price paid.

8.8 Notwithstanding any other provision of these Articles, if the Company issues any New Securities without consideration or for a consideration per share less than the Issue Price of any Preferred Share (a "**Qualifying Issue**"), then the Conversion Rate applicable to such Preferred Share immediately prior to such Qualifying Issue shall be adjusted such that the Conversion Rate in respect of such Preferred Share immediately following such Qualifying Issue ("**X**") shall be the product of the following formula:

$$X = \frac{OSP \times (ESC + NSC)}{(OSP \times ESC) + (ASP \times NSC)}$$

and for the purpose of this Article:

OSP is the Issue Price divided by the Conversion Rate of such Preferred Share immediately before the Qualifying Issue.

ESC is the total number of shares in the Company's equity share capital (as defined by the 2006 Act) that would be in issue on the date of conversion if all Shares the subject of all options, warrants, conversion rights (taking into account the then applicable Conversion Rate for the Preferred Shares) and all other rights of any person to acquire Shares granted by the Company prior to the Qualifying Issue had been exercised and the Shares the subject of such rights had been issued (but excluding any shares issued pursuant to the Qualifying Issue).

ASP is the average subscription price per New Security issued on the Qualifying Issue calculated by dividing the aggregate of amounts paid or to be paid in respect of the New Securities issued pursuant to the Qualifying Issue by the total number of New Securities issued pursuant to the Qualifying Issue.

NSC is the total number of shares issued pursuant to the Qualifying Issue.

8.9 For the avoidance of doubt, when a Preferred Shareholder holds Preferred Shares which have been issued at different Issue Prices, the adjustment to the Conversion Rate set out in Article 8.8 shall be applied separately to all of the Preferred Shares that have been issued at a particular Issue Price.

8.10 For the purposes of Article 8.8, the consideration received by the Company for the issue of New Securities shall be computed as follows:

(a) insofar as it consists in whole or in part of cash, the aggregate of the cash received by the Company for the issue of such New Securities; and

(b) insofar as it consists in whole or in part of property other than cash, the fair market value thereof at the time of such issue, as determined in good faith by the Board provided that if the holders of a majority of the relevant class of Preference Shares issued at the same Issue Price in whose favour the Conversion Rate is being adjusted pursuant to Article 8.8 disagree with such valuation the fair market value shall be determined by an umpire chosen by such holders of a majority of the relevant class of Preference Shares issued at the same Issue Price in whose favour the Conversion Rate is being adjusted pursuant to Article 8.8 and the Board and if they cannot agree on an umpire then on the application of any such Preferred Shareholder(s) by the President of the Institute of Chartered Accountants in England and Wales (and such umpire shall act as an expert and not as an arbitrator, his decision shall be final and binding save in the case of manifest error and his costs shall be met by the Company).

8.11 In the event that a Capital Reorganisation takes place whilst any Preferred Shares remain unconverted, the Auditors (acting as experts and not as arbitrators) shall determine whether it is necessary to adjust the Conversion Rate in respect of all those Preferred Shares to ensure that no Preferred Shareholder is in a worse position as a result of that Capital Reorganisation than he or it was in prior to that Capital Reorganisation taking place and, if so determined, the Conversion Rate shall be proportionately adjusted in such manner as is determined by the Auditors (acting as experts and not as arbitrators) to be fair and reasonable so as to achieve that objective. The Auditor's fees and expenses shall be paid by the Company.

8.12 If any Preferred Shareholder becomes entitled to a fraction of an Ordinary Share pursuant to any conversion of Preferred Shares under this Article 8, then his or its entitlement to Ordinary Shares on such conversion shall be rounded down to the nearest whole number.

9. VARIATION OF RIGHTS

Whenever the share capital of the Company is divided into different classes of shares, the special rights attached to any such class may only be varied or abrogated (either whilst the Company is a going concern or during or in contemplation of a winding-up) with the consent in writing of the holders of more than seventy five percent (75%) in nominal value of the issued shares of that class save that the rights (for the avoidance of doubt this will include class rights and any other rights) attaching to any class of Preferred Shares may only be varied or abrogated with the approval of A Ordinary Shareholders (where the rights of the A Ordinary Shareholders are being varied or abrogated) or B1 Ordinary Shareholders (where the rights of the B1 Ordinary Shareholders are being varied or abrogated) or B2 Ordinary Shareholders (where the rights of the B2 Ordinary Shareholders are being varied or abrogated), as applicable, holding more than seventy five percent (75%) of such number of Ordinary Shares considered to be held by such Shareholders of that class of Shares on an As Converted basis (by nominal value), where at least twenty five percent (25%) of the A Ordinary Shares (where the rights of the A Ordinary Shareholders are being varied or abrogated) or B1 Ordinary Shares (where the right of the B1 Ordinary Shareholders are being varied or abrogated) or B2 Ordinary Shares (where the rights of the B2 Ordinary Shareholders are being varied or abrogated) issued on or around the Date of Adoption remain in issue as at the date of such variation or abrogation.

10. ALLOTMENT OF NEW SHARES OR OTHER SECURITIES: PRE-EMPTION

10.1 In accordance with section 567(1) of the 2006 Act, sections 561(1) and 562(1) to (5) (inclusive) of the 2006 Act do not apply to an allotment of equity securities made by the Company.

10.2 Unless otherwise agreed in writing by a Preferred Majority, if the Company proposes to allot any New Securities those New Securities shall not be allotted to any person unless the Company has in the first instance offered them to all the Preferred Shareholders, on the same terms and at the same price as those New Securities are being offered to other persons on a pari passu and pro rata basis to the number of Ordinary Shares held by the Preferred Shareholders on an As Converted Basis (as nearly as may be without involving fractions). Any Preferred Shareholder may elect for a Member of the Same Fund Group or a Member of the Same Group to take up some or all of such offer on such Preferred Shareholder's behalf and subscribe for some or all of the relevant Preferred Shareholder's pro rata proportion in accordance with this Article.

10.3 The offer:

(a) shall be in writing, give details of the number and subscription price of the New Securities; and

(b) must be open for acceptance for a period of at least fifteen (15) Business Days; and

(c) shall stipulate that any Preferred Shareholder (or a Member of the Same Fund Group or a Member of the Same Group (as appropriate)) who wishes to subscribe for a number of New Securities in excess of the proportion to which each is entitled shall in their acceptance state the number of excess New Securities (the "**Excess Securities**") for which they wish to subscribe.

10.4 Any New Securities not accepted by the Preferred Shareholders pursuant to the offer made to them in accordance with Article 10.2 shall be used for satisfying any requests for Excess Securities made pursuant to Article 10.2 and in the event that there are insufficient Excess Securities to satisfy such requests, the Excess Securities shall be allotted to the applicants on a pro rata basis to the number of Ordinary Shares held by the applicants on an As Converted Basis immediately prior to the offer made to Preferred Shareholders in accordance with Article 10.2 (as nearly as may be without involving fractions or increasing the number allotted to any Shareholder beyond that applied for by him) and this process shall be repeated until all Excess Securities have been allotted or all requests for Excess Securities have been satisfied (whichever occurs sooner).

10.5 Any Excess Securities remaining after the application of Article 10.4 shall be offered, subject to Article 10.8, to any other person as the Directors may determine, on no more favourable terms (including as to price) as the offer to the Preferred Shareholders.

10.6 Subject to Articles 10.2, 10.3, 10.4 and 10.5 and to the provisions of section 551 of the 2006 Act, any New Securities shall be at the disposal of the Board who may allot, grant options over or otherwise dispose of them to any person at those times and generally on the terms and conditions they think proper, provided that the allotment to that person must be approved in writing by a Preferred Majority.

10.7 No Shares shall be allotted to any Employee, Director, prospective employee or director unless such person has entered into a joint section 431 ITEPA election with the Company.

10.8 In the event that a Preferred Majority consents to Shares being issued other than in accordance with Article 10.2 above, then such consent shall only be given in respect of Shares issued to persons who are not Investors (or any Member of the Same Fund Group or a Member of the Same Group) or Permitted Transferees of the Investors. Should the Company offer any Investor (or any Member of the Same Fund Group or a Member of the Same Group) or Permitted Transferee of any Investor the right to subscribe for any such Shares, then such offer must be extended to all the Investors in accordance with this Article 10 in respect of those Shares offered to such Investor (or any Member of the Same Fund Group or a Member of the Same Group) or Permitted Transferee.

10.9 Any New Securities offered under this Article 10 to CIC and/or a CIC Investor may be (with the prior approval of CIC and/or such CIC Investor (as applicable)) accepted in full or part by:

(a) a Member of the same Fund Group; or

(b) a Member of the same Group; or

(c) in the case of a CIC Investor, any other CIC Investor,

in each case in accordance with the terms of this Article 10.

11. LIEN

The Company shall have a first and paramount lien on every Share not fully paid for all and any indebtedness of any holder of it to the Company (whether a sole holder or one of two or more joint holders), whether or not that indebtedness or liability is in respect of the Shares concerned and whether or not it is presently payable.

12. TRANSFERS OF SHARES — GENERAL

12.1 In Articles 12 to 17 inclusive, reference to the transfer of a Share includes the transfer or assignment of a beneficial or other interest in that Share or the creation of a trust or encumbrance over that Share and reference to a Share includes a beneficial or other interest in a Share.

12.2 No Share may be transferred unless the transfer is made in accordance with these Articles.

12.3 If a Shareholder transfers or purports to transfer a Share otherwise than in accordance with these Articles he will be deemed immediately to have served a Transfer Notice in respect of all Shares held by him.

12.4 Any transfer of a Share by way of sale which is required to be made under Articles 14 to 18 (inclusive) will be deemed to include a warranty that the transferor sells with full title guarantee.

12.5 Unless express provision is made in these Articles to the contrary, and until a Sale or an IPO, no Ordinary Shares shall be transferred without the consent of a Preferred Majority.

12.6 In addition to the provisions of Regulation 24 of Table A, the Directors may refuse to register a transfer if:

(a) it is a transfer of a share to a bankrupt, a minor or a person of unsound mind; or

(b) the transfer is to an Employee, Director or prospective employee or director and such person has not entered in a joint section 431 ITEPA election with the Company,

and Regulation 24 of Table A shall be modified accordingly.

12.7 The Directors may, as a condition to the registration of any transfer of shares in the Company (whether pursuant to a Permitted Transfer or otherwise), require the transferee to execute and deliver to the Company a deed agreeing to be bound by the terms of any shareholders' agreement or similar document in force between some or all of the shareholders and the Company in any form as the Directors may reasonably require (but not so as to oblige the transferee to have any obligations or liabilities greater than those of the proposed transferor under any such agreement or other document) and if any condition is imposed in accordance with this Article the transfer may not be registered unless that deed has been executed and delivered to the Company's registered office by the transferee.

12.8 To enable the Directors to determine whether or not there has been any disposal of shares in the capital of the Company (or any interest in shares in the capital of the Company) in breach of these Articles the Directors may, with Investor Director Consent, require any holder or the legal personal representatives of any deceased holder or any person named as transferee in any transfer lodged for registration or any other person who the Directors or the Investor Directors may reasonably believe to have information relevant to that purpose, to furnish to the Company that information and evidence the Directors may request regarding any matter which they deem relevant to that purpose, including (but not limited to) the names, addresses and interests of all persons respectively having interests in the shares in the capital of the Company from time to time registered in the holder's name. If the information or evidence is not provided to enable the Directors to determine to their reasonable satisfaction that no breach has occurred, or where as a result of the information and evidence the Directors are reasonably satisfied that a breach has occurred, the Directors shall immediately notify the holder of such shares in the capital of the Company in writing of that fact and the following shall occur:

(a) the relevant shares shall cease to confer upon the holder of them (or any proxy) any rights:

(a) to vote whether on a show of hands or on a poll and whether exercisable at a general meeting of the Company or at any separate meeting of the class in question or by written resolution, provided that such rights shall not cease if as a result of such cessation the Company shall become a Subsidiary of a Preferred Shareholder; or

(b) to receive dividends or other distributions (other than the amount they may be entitled to pursuant to the application of Article 4.2) otherwise attaching to those shares or to any further shares issued in respect of those shares,

provided that the rights referred to in (a) above may be reinstated by the Board subject to Investor Director Consent.

12.9 In any case where the Board may require a Transfer Notice to be given in respect of any Shares, if a Transfer Notice is not duly given within a period of ten (10) Business Days of demand being made, a Transfer Notice shall be deemed to have been given at the expiration of that period. If a Transfer Notice is required to be given or is deemed to have been given under these Articles then (unless provided otherwise in these Articles), the Transfer Notice will be treated as having specified that:

(a) the proposed transferee is the Company;

(b) the Transfer Price for the Sale Shares will be the proposed price agreed between the Seller and the proposed transferee (or in the absence of such agreement, as determined by the Board with Investor Director Consent);

(c) it does not include a Minimum Transfer Condition (as defined in Article 14.2(d)); and

(d) the Seller wishes to transfer all of the Shares held by it.

13. PERMITTED TRANSFERS

13.1 Subject to Article 12.5, a Shareholder (the "**Original Shareholder**") may transfer all or any of his or its Shares to a Permitted Transferee without restriction as to price or otherwise.

13.2 Where under the provision of a deceased Shareholder's will or laws as to intestacy, the persons legally or beneficially entitled to any Shares, whether immediately or contingently, are Permitted Transferees of the deceased Shareholder, the legal representative of the deceased Shareholder may transfer any Share to those Permitted Transferees, in each case without restriction as to price or otherwise. Shares previously transferred as permitted by this Article 13.2 may be transferred by the transferee to any other Permitted Transferee of the Original Shareholder without restriction as to price or otherwise.

13.3 If a Permitted Transferee who was a Member of the Same Group as the Original Shareholder ceases to be a Member of the Same Group as the Original Shareholder, the Permitted Transferee must not later than five (5) Business Days after the date on which the Permitted Transferee so ceases, transfer the Shares held by it to the Original Shareholder or a Member of the Same Group as the Original Shareholder (which in either case is not in liquidation) without restriction as to price or otherwise failing which it will be deemed to have given a Transfer Notice in respect of those Shares.

13.4 If a Permitted Transferee who was a Member of the Same Fund Group as the Original Shareholder ceases to be a Member of the Same Fund Group as the Original Shareholder, the Permitted Transferee must not later than five (5) Business Days after the date on which the Permitted Transferee so ceases, transfer the Shares held by it to the Original Shareholder or a Member of the Same Fund Group as the Original Shareholder (which in either case is not in liquidation) without restriction as to price or otherwise failing which it will be deemed to give a Transfer Notice in respect of such Shares.

13.5 Shares previously transferred by any Investor as permitted by Article 13.1 may be transferred by the transferee to any other Permitted Transferee of the Original Shareholder without restriction as to price or otherwise.

13.6 A transfer of any Shares approved by a Preferred Majority may be made without restriction as to price or otherwise and each such transfer shall be registered by the Directors. In the event that a Preferred Majority has approved Shares being transferred without restriction, then such approval shall only be given in respect of Shares transferred to persons who are not Investors (or any Member of the Same Fund Group or a Member of the Same Group) or Permitted Transferees of Investors. Should the Seller offer any Investor (or any Member of the Same Fund Group or a Member of the Same Group) or Permitted Transferee of any Investor the right to acquire any Shares, then such offer must be extended to all the Investors in accordance with Article 10 in respect of those Shares being offered to any Investor (or any Member of the Same Fund Group or a Member of the Same Group) or Permitted Transferee of any Investor.

13.7 Trustees may (i) transfer Shares to a company in which they hold the whole of the share capital and which they control (a "**Qualifying Company**") or (ii) transfer Shares to the Original Shareholder or to another Permitted Transferee of the Original Shareholder or (iii) transfer Shares to the new or remaining Trustees upon a change of Trustees without restrictions as to price or otherwise.

13.8 No transfer of Shares may be made to Trustees unless the Board is satisfied:

(a) with the terms of the trust instrument and in particular with the powers of the trustees;

(b) with the identity of the proposed trustees;

(c) the proposed transfer will not result in fifty percent (50%) or more of the aggregate of the Company's equity share capital being held by trustees of that and any other trusts; and

(d) that no costs incurred in connection with the setting up or administration of the Family Trust in question are to be paid by the Company.

13.9 If a company to which a Share has been transferred under Article 13.7, ceases to be a Qualifying Company it must within five (5) Business Days of so ceasing, transfer the Shares held by it to the Trustees or to a Qualifying Company (any may do so without restriction as to price or otherwise) failing which it will be deemed to have given a Transfer Notice in respect of such Shares.

13.10 If a Permitted Transferee who is a spouse or Civil Partner of the Original Shareholder ceases to be a spouse or Civil Partner of the Original Shareholder whether by reason of divorce or otherwise he must, within fifteen (15) Business Days of so ceasing either:

(a) execute and deliver to the Company a transfer of the Shares held by him to the Original Shareholder (or, to any Permitted Transferee of the Original Shareholder) for such consideration as may be agreed between them; or

(b) give a Transfer Notice to the Company in accordance with Article 14.2; failing which he shall be deemed to have given a Transfer Notice.

13.11 On the death (subject to Article 13.2), bankruptcy, liquidation, administration or administrative receivership of a Permitted Transferee (other than a joint holder) his personal representatives or trustee in bankruptcy, or its liquidator, administrator or administrative receiver must within five (5) Business Days after the date of the grant of probate, the making of the bankruptcy order or the appointment of the liquidator, administrator or the administrative receiver execute and deliver to the Company a transfer of the Shares held by the Permitted Transferee without restriction as to price or otherwise. The transfer shall be to the Original Shareholder if still living (and not bankrupt or in liquidation) or, if so directed by the Original Shareholder, to any Permitted Transferee of the Original Shareholder. If the transfer is not executed and delivered within five (5) Business Days of such period or if the Original Shareholder has died or is bankrupt or is in liquidation, the personal representative or trustee in bankruptcy or liquidator will be deemed to have given a Transfer Notice.

14. TRANSFERS OF SHARES SUBJECT TO PRE-EMPTION RIGHTS

14.1 Save in the case of Permitted Transfers, transfers of Shares made pursuant to any offer extended to Shareholders pursuant to Article 16, transfers of Sellers' Shares and Called Shares pursuant to Article 17 and purchases by the Company of its own shares under Article 15.5 and/or Article 18, any transfer of Shares by a Shareholder shall be subject to the pre-emption rights contained in this Article 14.

14.2 Subject always to Article 14.9(f), a Shareholder who wishes to transfer Shares (a "**Seller**") shall, except as otherwise provided in these Articles, before transferring or agreeing to transfer any Shares give notice in writing (a "**Transfer Notice**") to the Company specifying:

(a) the number of Shares which he wishes to transfer (the "**Sale Shares**");

(b) if he wishes to sell the Sale Shares to a third party, the name of the proposed transferee (the "**Proposed Buyer**");

(c) the price (in cash) at which he wishes to transfer the Sale Shares (the "**Transfer Price**"); and

(d) whether the Transfer Notice is conditional on all or a specific number of the Sale Shares being sold to Shareholders (a "**Minimum Transfer Condition**").

14.3 Except with the Investor Director Consent, no Transfer Notice once given or deemed to have been given under these Articles may be withdrawn.

14.4 A Transfer Notice constitutes the Company the agent of the Seller for the sale of the Sale Shares at the Transfer Price.

14.5 As soon as practicable following the receipt of a Transfer Notice the Board shall offer the Sale Shares for sale to the Shareholders in the manner set out in Articles 14.6 to 14.8. Each offer must be in writing and give details of the number and Transfer Price of the Sale Shares offered.

14.6 *Priority for offer of Sale Shares*

The Company shall offer the Sale Shares in the following priority:

(a) first, to the Preferred Shareholders (pro rata to the number of Ordinary Shares each Preferred Shareholder holds on an As Converted Basis as a proportion of all Ordinary Shares held by Preferred Shareholders on an As Converted Basis); and

(b) second, to the Ordinary Shareholders;

in each case on the basis as set out in Article 14.7 and Article 14.8.

14.7 *Transfers: First Offer*

(a) In accordance with the priority rights contained in Article 14.6, the Board shall offer the Sale Shares to all the Preferred Shareholders (other than the Seller) by notice in writing inviting them to apply in writing for the maximum number of Sale Shares they wish to buy.

(b) The Preferred Shareholders shall be invited to apply in writing within the period from the date of the offer to the date fifteen (15) Business Days after the offer (inclusive) (the "**First Offer Period**").

(c) If, at the end of the First Offer Period, the number of Sale Shares applied for is more than or equal to the total number of Sale Shares, the Board shall allocate the Sale Shares to each Preferred Shareholder in the proportion (fractional entitlements being rounded to the nearest whole number) which his existing holding of Ordinary Shares (calculated on an As Converted Basis) bears to the total number of Ordinary Shares held by those Preferred

Shareholders (calculated on an As Converted Basis) who have applied during the First Offer Period for Sale Shares but no allocation shall be made to a Preferred Shareholder of more than the maximum number of Sale Shares which he has stated he is willing to buy. Further allocations shall be made on the same basis until all of the Sale Shares have been allocated or, if sooner, all applications by Preferred Shareholders for Sale Shares have been satisfied.

(d) If, at the end of the First Offer Period, the number of Sale Shares applied for is less than the total number of Sale Shares, the Board shall offer the balance to the Ordinary Shareholders (other than the Seller), in accordance with the priority rights in Article 14.6, who shall be invited to apply in writing within the period from the date of that offer to the date fifteen (15) Business Days after that offer (inclusive) (the "**Second Offer Period**").

(e) If, at the end of the Second Offer Period, the number of Sale Shares applied for is more than or equal to the balance of Sale Shares following the First Offer Period (the

"**Second Offer Sale Shares**"), the Board shall allocate the Second Offer Sale Shares to each Ordinary Shareholder in the proportion (fractional entitlements being rounded to the nearest whole number) which his existing holding of Ordinary Shares bears to the total number of Ordinary Shares held by those Ordinary Shareholders who have applied during the Second Offer Period for Second Offer Sale Shares but no allocation shall be made to an Ordinary Shareholder of more than the maximum number of Second Offer Sale Shares which he has stated he is willing to buy. Further allocations shall be made on the same basis until all of the Second Offer Sale Shares have been allocated or, if sooner, all applications by Preferred Shareholders for Second Offer Sale Shares have been satisfied.

(f) If, at the end of the Second Offer Period, the total number of Sale Shares applied for by both the Preferred Shareholders and the Ordinary Shareholders (other than the Seller) (the "**Continuing Shareholders**") is less than the number of Sale Shares, the Board shall allocate the Sale Shares to such Shareholders in accordance with their respective applications and the overall balance (the "**Initial Surplus Shares**") will be dealt with in accordance with Article 14.8.

(g) If the Sale Shares are subject to a Minimum Transfer Condition then any allocation made under this Article 14.7 and Article 14.8 will be conditional on the fulfilment of the Minimum Transfer Condition.

14.8 *Transfers: Second Offer*

(a) At the end of the Second Offer Period, the Board shall offer the Initial Surplus Shares to all the Continuing Shareholders inviting them to apply in writing within the period from the date of the offer to the date fifteen (15) Business Days after the date of the offer (inclusive) (the "**Third Offer Period**") for the maximum number of the Initial Surplus Shares they wish to buy.

(b) If, at the end of the Third Offer Period, the number of Initial Surplus Shares applied for is equal to or exceeds the number of Initial Surplus Shares, the Board shall allocate the remaining Initial Surplus Shares to each Continuing Shareholder in the proportion (fractional entitlements being rounded to the nearest whole number) which his existing holding of Ordinary Shares bears to the total number of Ordinary Shares (assuming that the Preferred Shareholders which constitute Continuing Shareholders hold Ordinary Shares on an As Converted Basis) held by those Continuing Shareholders who have applied during the Third Offer Period for Initial Surplus Shares but no allocation shall be made to a Shareholder of more than the maximum number of Initial Surplus Shares which he has stated he is willing to buy. Further allocations shall be made on the same basis until all of the Initial Surplus Shares have been allocated or, if sooner, all applications by Continuing Shareholders for Initial Surplus Shares have been satisfied.

(c) If, at the end of the Third Offer Period, the number of Initial Surplus Shares applied for is less than the number of Initial Surplus Shares, the Board shall allocate the Initial Surplus Shares to the Continuing Shareholders in accordance with their applications and the balance (the "**Second Surplus Shares**") will be offered to any other person in accordance with 14.9(e).

14.9 *Completion of transfer of Sale Shares*

(a) If the Transfer Notice includes a Minimum Transfer Condition and the total number of Shares applied for by Shareholders is less than the number of Sale Shares specified in the Minimum Transfer Condition, the Board shall notify the Seller and all those to whom Sale Shares have been conditionally allocated under Articles 14.7 and 14.8 stating that the Minimum Transfer Condition has not been met and that the offers to Shareholders and allocations made under this Article 14 have lapsed with immediate effect, and the provisions of Article 14.9(e) shall instead apply.

(b) If:

(a) the Transfer Notice does not include a Minimum Transfer Condition; or

(b) the Transfer Notice does include a Minimum Transfer Condition but allocations have been made in respect of all or the minimum required number of the Sale Shares,

the Board shall, when no further offers are required to be made under Articles 14.7 and 14.8, give written notice of allocation (an "**Allocation Notice**") to the Seller and each party to whom Sale Shares have been allocated (an "**Applicant**") specifying the number of Sale Shares allocated to each Applicant and the place and time (being not less than ten (10) Business Days nor more than twenty (20) Business Days after the date of the Allocation Notice) for completion of the transfer of the Sale Shares.

(c) Upon service of an Allocation Notice, the Seller must, against payment of the Transfer Price, transfer the Sale Shares in accordance with the requirements specified in it.

(d) If the Seller fails to comply with the provisions of Article 14.9(c):

(a) the Chairman of the company or, failing him, one of the directors, or some other person nominated by a resolution of the Board, may on behalf of the Seller:

(A) complete, execute and deliver in his name all documents necessary to give effect to the transfer of the relevant Sale Shares to the Applicants;

(B) receive the Transfer Price and give a good discharge for it; and

(C) (subject to the transfer being duly stamped) enter the Applicants in the register of Shareholders as the holders of the Sale Shares purchased by them; and

(b) the Company shall pay the Transfer Price into a separate bank account in the Company's name on trust (but without interest) for the Seller until he has delivered to the Company his certificate or certificates for the relevant Shares (or an indemnity, in a form reasonably satisfactory to the Board, in respect of any lost certificate).

(e) If an Allocation Notice does not relate to all the Sale Shares then, subject to Article 14.9(f), the Seller may, within eight (8) weeks after service of the Allocation Notice, transfer the Second Surplus Shares to the Proposed Buyer at a price at least equal to the Transfer Price. If Article 14.9(a) applies, then subject to Article 14.9(f), the Seller may, within eight (8) weeks after the date of the notice from the Board served under Article 14.9(a), transfer some or all of the Sale Shares to the Proposed Buyer at a price at least equal to the Transfer Price, provided that the number of Sale Shares so transferred must be not less than the number of Sale Shares specified in the Minimum Transfer Condition.

(f) The right of the Seller to transfer Shares under this Article 14 does not apply if the Board is of the opinion on reasonable grounds that:

(a) the transferee is a person (or a nominee for a person) whom the Directors (with Investor Director Consent) determines in their absolute discretion is a

competitor with (or an Associate of a competitor with) the business of the Company or with a Subsidiary Undertaking of the Company;

(b) the sale of the Sale Shares is not bona fide or the price is subject to a deduction, rebate or allowance to the transferee; or

(c) the Seller has failed or refused to provide promptly information available to it or him and reasonably requested by the Board for the purpose of enabling it to form the opinion mentioned above.

15. COMPULSORY TRANSFERS AND SHARE BUYBACK

15.1 A person entitled to a Share in consequence of the bankruptcy of a Shareholder shall be deemed to have given a Transfer Notice in respect of that Share at a time determined by the Directors.

15.2 If a Share remains registered in the name of a deceased Shareholder for longer than one (1) year after the date of his death the Directors may require the legal personal representatives of that deceased Shareholder either:

(a) to effect a Permitted Transfer of such Shares (including for this purpose an election to be registered in respect of the Permitted Transfer); or

(b) to show to the satisfaction of the Directors that a Permitted Transfer will be effected before or promptly upon the completion of the administration of the estate of the deceased Shareholder,

and if either requirement in this Article shall not be fulfilled to the satisfaction of the Directors a Transfer Notice shall be deemed to have been given in respect of each such Share, save to the extent that the Directors may otherwise determine.

15.3 If a Shareholder which is a company or a Permitted Transferee of that Shareholder, either suffers or resolves for the appointment of a liquidator, administrator or administrative receiver over it or any material part of its assets, the relevant Shareholder or Permitted Transferee shall be deemed to have given a Transfer Notice in respect of all the shares held by the relevant Shareholder and/or such Permitted Transferee save to the extent that, and at a time, the Directors may determine.

15.4 If there is a change in control (as control is defined in section 1124 of the Corporation Tax Act 2010) of any Shareholder, or any Permitted Transferee of a Shareholder which in each case is a company, it shall be bound at any time, if and when required in writing by the Directors to do so, to give (or procure the giving in the case of a nominee) a Transfer Notice in respect of all the Shares registered in its name and its nominees' names save that, in the case of any Permitted Transferee, it shall first be permitted to transfer those Shares back to the Original Shareholder from whom it received its Shares or to any other Permitted Transferee before being required to serve a Transfer Notice. This Article shall not apply to a member that is a Preferred Shareholder or to UKRI.

Employees

15.5 If any Employee ceases for any reason to be an Employee at any time, or if any Former Employee owns any Employee Shares and becomes a Bad Leaver, the relevant holder of Employee Shares shall be deemed to have given a notice in writing to the Company of his intention to transfer such proportion of the Employee Shares as set forth in this Article 15.5 to the Company (the "**Transfer Notice**") on the Effective Termination Date, or on the date a Former Employee holding Employee Shares is determined to be a Bad Leaver (the "**Bad Leaver Date**"), unless or to the extent the Board with Investor Director Consent otherwise resolves or directs in writing in respect of any such Employee Shares prior to or within ten (10) Business Days after the relevant Effective Termination Date or the Bad Leaver Date. In

respect of each Transfer Notice which is deemed to have been served under this Article 15.5, the proportion of the Employee Shares and the applicable Transfer Price shall be as follows:

(a) where the relevant Employee is, or the Former Employee is, a Bad Leaver, 100% of the Employee Shares held by such Employee or Former Employee for an aggregate consideration of £1.00; or

(b) where the relevant Employee ceases to be an Employee but is not a Bad Leaver, the Leaver's Percentage of Employee Shares held by such Employee for an aggregate consideration of £1.00.

15.6 Any Employee or Former Employee that has been deemed to have given a Transfer Notice pursuant to Article 15.5 will be required within 10 Business Days after the Effective Termination Date or the Bad Leaver Date (as applicable) to enter into and deliver a buyback agreement to the Company (the "**Buyback Agreement**"), a signed and completed stock transfer form in respect of those Employee Shares being compulsorily transferred and/or an indemnity for lost share certificate (if applicable). Such Buyback Agreement shall include (at a minimum):

(a) a requirement for the Employee or Former Employee (as applicable) to transfer such number of Employee Shares as determined in accordance with Article 15.5(a) or 15.5(b) (as applicable) to the Company for the applicable transfer price (which for the avoidance of doubt, shall be £1.00 in total for all Employee Shares being compulsorily transferred to the Company by any Employee or Former Employee);

(b) warranties given by the Employee or Former Employee (as applicable) that they have good title to the Employee Shares and the capacity and authority to transfer the Employee Shares; and

(c) a requirement for the Employee or Former Employee (as applicable) to deliver to the Company a share certificate or a signed indemnity for lost share certificate and a signed stock transfer form in respect of the relevant Employee Shares.

15.7 If an Employee or Former Employee fails to sign and deliver to the Company any or all of the Buyback Agreement, the stock transfer form and/or the share certificate (or a suitable indemnity for lost share certificate) for his Employee Shares being compulsorily transferred to the Company in accordance with the terms of this Article 15 and the Buyback Agreement, any Director may act as agent of the relevant Employee or Former Employee and shall be empowered to enter into any such agreements, documents or deeds on behalf of the Employee or Former Employee to effect the transfer of the Employee Shares to the Company in accordance with this Article 15. The Board shall then authorise registration of the transfer once appropriate stamp duty (if any) has been paid.

15.8 All voting rights attached to Employee Shares held by an Employee, Former Employee or their respective Permitted Transferees (the "**Restricted Member**"), if any, shall from the Effective Termination Date or the Bad Leaver Date (as applicable), be suspended unless the Board (acting with the consent of the Preferred Majority) notifies him otherwise.

15.9 The Board, with Investor Majority Consent, may at any time prior to the transfer of any Employee Shares pursuant to a Transfer Notice which is deemed to have been served in accordance with Article 15.5, dis-apply the application of Articles 15.5 to 15.8 (and thereby exclude them from the Transfer Notice) in relation to some or all of the Employee Shares which are the subject of such Transfer Notice.

16. TAG ALONG

16.1 Subject to Article 16.3, in the case of any transfer or series of transfers by a Shareholder (the "**Selling Shareholder**") of Shares (the "**Sale Shares**") pursuant to an offer which would result in the proposed purchaser(s) holding between ten percent (10%) and fifty percent (50%) of the share capital on an As Converted Basis, the Selling Shareholder will notify each Preferred Shareholder in writing at least ten (10) Business Days prior to the completion of such transfer(s) and any Preferred Shareholder may within that period require that such Selling Shareholder will not sell any such Shares unless the proposed purchaser(s) of such Shares:

(a) shall have offered to purchase from the Preferred Shareholders at the price per Ordinary Share offered by the proposed purchaser(s), calculated on As Converted Basis (the "**Prescribed Price**") such proportion of the Ordinary Shares held by each Preferred Shareholder (calculated on an As Converted Basis) as is equal to the proportion which the Sale Shares bears to the Selling Shareholders' total shareholding (including the Shares to be sold, and calculated on an As Converted Basis) (the "**Prescribed Portion**"); and

(b) shall, in respect of any Preferred Shareholder that wishes to take up the offer referred to in Article 16.1(a) above, acquire from such Shareholder in question the Prescribed Proportion of his Shares at the Prescribed Price simultaneously with the acquisition from the Selling Shareholder of the Sale Shares to be sold.

16.2 In the case of any transfer or series of transfers pursuant to an offer which would result in the proposed purchaser(s) holding more than fifty percent (50%) of the issued Shares of the Company on an As Converted Basis, the Selling Shareholder will not sell any such Sale Shares under this Article unless the proposed purchaser(s) of such Shares:

(a) shall have offered to purchase from all the other Shareholders (at the Prescribed Price) all of the Shares held by each such Shareholder; and

(b) shall, in respect of any Shareholder which wishes to take up the offer referred to in Article 16.2(a) above, acquire from such holder the Shares in question at the relevant price simultaneously with the acquisition from the Selling Shareholder of the Sale Shares to be sold.

16.3 This Article 16 shall not apply to:

(a) Permitted Transfers;

(b) Compulsory Transfers; and

(c) any transfer or series of transfers of Sellers' Shares in connection with which the Drag Along Option has been exercised.

17. DRAG ALONG

17.1 Notwithstanding the provisions of Articles 14.2 and 16, if Shareholders comprising a Super Preferred Majority wish to transfer all of their interest in Shares (the "**Sellers' Shares**") to a third party Proposed Purchaser pursuant to a Bona Fide Offer, the Selling Shareholders shall have the option (the "**Drag Along Option**") to require all the other holders of Shares (the "**Called Shareholders**") to sell and transfer all their Shares to the Proposed Purchaser or as the Proposed Purchaser shall direct in accordance with the provisions of this Article.

17.2 Selling Shareholder(s) may exercise the Drag Along Option by giving a written notice to that effect (a "**Drag Along Notice**") to the Called Shareholders at any time before the transfer of the Sellers' Shares to the Proposed Purchaser. A Drag Along Notice shall specify that the Called Shareholders are required to transfer all their Shares (the "**Called Shares**") under this

Article, the person to whom they are to be transferred, the consideration for which the Called Shares are to be transferred (calculated in accordance with this Article) and the proposed date of transfer.

17.3 Drag Along Notices shall be irrevocable but will lapse if for any reason there is not a sale of the Sellers' Shares by the Selling Shareholder(s) to the Proposed Purchaser within forty (40) Business Days after the date of service of the Drag Along Notice. The Selling Shareholder(s) shall be entitled to serve further Drag Along Notices following the lapse of any particular Drag Along Notice.

17.4 The consideration (in cash or otherwise) for which the Called Shareholders shall be obliged to sell each of the Called Shares shall be that to which they would be entitled if the total consideration proposed to be paid by the Proposed Purchaser were distributed to the holders of the Called Shares and the Sellers' Shares in accordance with Article 5.

17.5 No Drag Along Notice may require a Called Shareholder to agree to any terms except: (a) that such Called Shareholder has the authority to transfer the Called Shares, is the legal and beneficial owner of the Called Shares and has good and valid title to the Called Shares, free and clear of any and all encumbrances; (b) that the transfer of the Called Shares does not violate any agreement to which such Called Shareholder is a party or by which it is bound; and (c) to the extent securities are offered, in whole or in part, as consideration in the Bona Fide Offer, such customary representations as may be required under any applicable laws or by any applicable regulatory authority to ensure that the Called Shareholder may lawfully be offered or acquire such securities.

17.6 Within five (5) Business Days of the Selling Shareholders serving a Drag Along Notice on the Called Shareholders, the Called Shareholders shall deliver stock transfer forms for their shares in favour of the Proposed Purchaser or as the Proposed Purchaser shall direct, together with the relevant share certificate(s) (or a suitable indemnity in lieu thereof) to the Company. As soon as reasonably possible after the documents referred to in this Article have been delivered to the Company by or on behalf of the Called Shareholders, the Company shall pay the Called Shareholders, on behalf of the Proposed Purchaser, the amounts they are due pursuant to Article 17.4 to the extent the Proposed Purchaser has put the Company in the requisite funds. The Company's receipt for the price shall be a good discharge to the Purchaser. The Company shall hold the amounts due to the Called Shareholders pursuant to Article 17.4 in trust for the Called Shareholders without any obligation to pay interest.

17.7 To the extent that the Proposed Purchaser has not, on the expiration of the forty (40) Business Day period referred to in Article 17.3, put the Company in funds to pay the price due pursuant to Article 17.6, the Called Shareholders shall be entitled to the return of the stock transfer forms and share certificate (or suitable indemnity) for the relevant shares and the Called Shareholders shall have no further rights or obligations under this Article 17 in respect of their shares.

17.8 If a Called Shareholder fails to deliver stock transfer forms and share certificates (or suitable indemnity) for its shares to the Company upon the expiration of the five (5) Business Day period referred to in Article 17.6, the Directors shall, if requested by the Proposed Purchaser, authorise any Director to transfer the Called Shareholders shares on the Called Shareholder's behalf to the Proposed Purchaser (or its nominee(s)) to the extent the Proposed Purchaser has, at the expiration of that five (5) Business Day period, put the Company in funds to pay the price for the Called Shareholder's shares offered to him. The Board shall then authorise registration of the transfer once appropriate stamp duty has been paid. The defaulting Called Shareholder shall surrender his share certificate for his shares (or provide a suitable indemnity) to the Company. On surrender, he shall be entitled to the amount due to him under Article 17.4.

17.9 Any transfer of Seller's Shares or Called Shares to a Proposed Purchaser (or as they may direct) pursuant to a sale in respect of which a Drag Along Notice has been duly served shall not be subject to the provisions of Article 14 or Article 16.

17.10 On any person, at any time following the issue of a Drag Along Notice, becoming a Shareholder of the Company pursuant to the exercise of a pre-existing option to acquire shares in the Company or pursuant to the conversion of any convertible security of the Company (a "**New Shareholder**"), a Drag Along Notice shall be deemed to have been served on the New Shareholder on the same terms as the previous Drag Along Notice who shall then be bound to sell and transfer all Shares so acquired to the Proposed Purchaser or as the Proposed Purchaser may direct and the provisions of this Article shall apply with the necessary changes to the New Shareholder except that completion of the sale of the Shares shall take place immediately on the Drag Along Notice being deemed served on the New Shareholder.

18. NEW HOLDING COMPANY

18.1 In the event of a Holding Company Reorganisation approved by (i) the Board and (ii) a Super Preferred Majority, (a "**Proposed Reorganisation**"), all Shareholders shall (i) consent to, vote for, raise no objections to and waive any applicable rights in connection with the Proposed Reorganisation and (ii) take all necessary actions to tender their Shares required to effect the Proposed Reorganisation (the "**Reorganisation Actions**"). The Shareholders shall be required to take all Reorganisation Actions with respect to the Proposed Reorganisation as are necessary and required by the Board and approved by a Super Preferred Majority to facilitate the Proposed Reorganisation provided that nothing in this Article 18.1 shall require any Shareholder to take any unlawful action or step. If any Shareholder fails to comply with the provisions of this Article, the Company shall be constituted the agent of each defaulting Shareholder for taking the Reorganisation Actions as are necessary to effect the Proposed Reorganisation and the Directors may authorise an officer or member to execute and deliver on behalf of such defaulting Shareholder the necessary documents to effect the Proposed Reorganisation, including, without limitation, any share exchange agreement and/or stock transfer form.

18.2 The Company shall procure that the Holding Company shall ensure that the shares issued by it to the Shareholders (or a subsequent holder, as the case may be) pursuant to the Holding Company Reorganisation will be credited as fully paid and which new shares shall be subject to the constitutional documents of the Holding Company and otherwise (subject to the express provisions of such constitutional documents) have the same rights as all other Holding Company shares of the same class in issue at the time.

18.3 On any person, following the date of completion of a Holding Company Reorganisation, becoming a Shareholder pursuant to the exercise of a pre-existing option or Warrant to acquire shares in the Company or pursuant to the conversion of any convertible security of the Company or otherwise (a "**New Reorganisation Shareholder**"), the New Reorganisation Shareholder shall then be bound to do all such acts and things necessary in order to transfer all such resulting shares to the Holding Company, and the provisions of this Article shall apply with the necessary changes to the New Reorganisation Shareholder provided that nothing in this Article 18.3 shall require any such New Reorganisation Shareholder to take any unlawful action or step.

19. PURCHASE OF SHARES

19.1 Subject to the 2006 Act but without prejudice to any other provision of these Articles, the Company may purchase its own shares in accordance with Chapter 4 of Part 18 of the 2006 Act up to any amount in a financial year not exceeding the lower of:

(a) £15,000; and

(b) the nominal value of 5% of the Company's fully paid share capital at the beginning of each financial year of the Company.

19.2 Where the Directors exercise the Company's power to purchase its own shares in accordance with Chapter 4 of Part 18 of the 2006 Act:

(a) those shares bought back will be treated as cancelled; and

(b) the amount of the Company's issued share capital is diminished accordingly by the nominal amount of the shares cancelled (in accordance with section 706 of the 2006 Act).

19.3 Subject to the 2006 Act but without prejudice to any other provision of these Articles, the Company shall be authorised, for a period expiring on the fifth anniversary of the Date of Adoption, to purchase its own shares up to a limit of 100,000 shares for a minimum price of £0.00001 and a maximum price of £1.00 per share for the purposes of or pursuant to an employee share scheme in accordance with section 693A of the 2006 Act.

19.4 Article 12.5 does not apply to this Article 19.

20. GENERAL MEETINGS

The Directors may call general meetings and, on the requisition of members pursuant to the provisions of the 2006 Act, shall forthwith proceed to convene a general meeting in accordance with the provisions of the 2006 Act.

21. PROXIES

The instrument appointing a proxy and any authority under which it is executed or a copy of such authority certified notarially or in some other way approved by the Directors may:

(a) be deposited at the office or at any other place within the United Kingdom as may be specified in the notice convening the meeting or in any instrument of proxy sent out by the Company in relation to the meeting at any time before the time for holding the meeting or adjourned meeting at which the person named in the instrument proposes to vote;

(b) be delivered at the meeting or adjourned meeting at which the person named in the instrument proposes to vote to the Chairman or to the Secretary or to any Director; or

(c) in the case of a poll, be delivered at the meeting at which the poll was demanded to the Chairman or to the Secretary or to any Director, or at the time and place at which the poll is held to the Chairman or to the Secretary or to any Director or scrutineer,

and an instrument of proxy which is not deposited or delivered in a manner so permitted shall be invalid.

22. DIRECTORS' BORROWING POWERS

The Directors may exercise all the powers of the Company to borrow or raise money and to mortgage or charge its undertaking, property and uncalled capital and to issue debentures, debenture stock and other securities as security for any debt, liability of obligation of the Company or of any third party.

23. ALTERNATE DIRECTORS

Notwithstanding any provision of these Articles to the contrary, any person appointed as a Director by an Investor may appoint any person as he or she thinks fit to be his or her or its alternate director and the appointment of an alternate director shall not require approval by a resolution of the Directors, and in its application to the Company Regulation 65 of Table A shall be modified accordingly.

24. NUMBER OF DIRECTORS

Unless and until the Company in general meeting shall otherwise determine the number of Directors shall not be less than three (3) and not more than ten (10), save where determined by the Board and a Preferred Majority.

25. APPOINTMENT OF DIRECTORS

25.1 For so long as Atlas and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as Atlas may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by Atlas or otherwise, to appoint another Director in his place.

25.2 For so long as Novartis and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as Novartis may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by Novartis or otherwise, to appoint another Director in his place.

25.3 For so long as S.R. One and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as S.R. One may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by S.R. One or otherwise, to appoint another Director in his place.

25.4 For so long as SVLSA and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as SVLSA may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by SVLSA or otherwise, to appoint another Director in his place.

25.5 For so long as Vertex and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as Vertex may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by Vertex or otherwise, to appoint another Director in his place.

25.6 For so long as CIC and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as CIC may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by CIC or otherwise, to appoint another Director in his place.

25.7 For so long as Tyboume and/or its Permitted Transferees hold Shares, they shall have the right to appoint and maintain in office such natural person as Tybourne may from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by Tybourne or otherwise, to appoint another Director in his place.

25.8 For so long as the Founders hold Shares, they shall have the right to appoint and maintain in office such natural person as the Founders shall from time to time nominate as a Director of the Company (and as a member of each and any committee of the Board) and to remove any Director so appointed and, upon his removal whether by the Founders or otherwise, to appoint another Director in his place.

25.9 The Ordinary Shareholders shall have the right to appoint as a Director the then current Chief Executive Officer of the Company and (with the consent of a Preferred Majority) to remove him as a Director and, with the consent of the Preferred Majority, to appoint any replacement Chief Executive Officer as a Director in his place. Upon the resignation of removal of the Chief Executive Officer from his executive position at the Company, the Ordinary

Shareholders shall, if directed to do so by a Preferred Majority, remove the former Chief Executive Officer as a Director.

25.10 The Directors appointed pursuant to Articles 25.1 to 25.7 shall have the right to appoint and maintain in office one (1) Independent Director and to remove any Director so appointed and, upon his removal whether by the Directors or otherwise, to appoint another Independent Director in his place.

25.11 For so long as Longwood and/or its Permitted Transferees hold Shares, it shall be entitled to appoint (and remove) by notice in writing to the Company a representative (the "**Longwood Observer**") to attend as an observer at each and any meeting of the Board and of each and any committee of the Board and to remove any Longwood Observer so appointed, upon his removal whether by Longwood or otherwise, to appoint another Longwood Observer in his place. For so long as Ahren and/or its Permitted Transferees hold Shares, it shall be entitled to appoint (and remove) by notice in writing to the Company a representative (the "**Ahren Observer**") to attend as an observer at each and, with the consent of all of the Investor Directors (which shall not be unreasonably withheld), any meeting of the Board and of each and any committee of the Board and to remove any Ahren Observer so appointed, upon his removal whether by Ahren or otherwise, to appoint another Ahren Observer in his place.

25.12 In its application to the Company Regulation 78 of Table A shall be modified by the deletion of the words "*...and may also determine the rotation in which any additional Directors are to retire*".

25.13 In its application to the Company, Regulation 84 of Table A shall be modified by the deletion of the third and final sentences.

25.14 Notwithstanding any other provision of these Articles, on any resolution which is proposed in general meeting (either on a show of hands or on a poll) to remove a Director appointed in accordance with Articles 25.1 to 25.11 from office or any resolution proposed in general meeting (either on a show of hands or on a poll) or as a written resolution to alter the Articles so as to result in the deletion or amendment of Articles 25.1 to 25.11, the votes cast by the members (or the duly appointed proxies or corporate representatives of the members) entitled to appoint and remove any Director(s) or observers under the affected Articles shall, if voting against that resolution, in aggregate carry a number of votes equal to 50.01% of the number of votes capable of being cast on that resolution.

26. DIRECTORS' PERMITTED INTERESTS

26.1 Provided that he has declared the nature and extent of his interest in accordance with (and to the extent required by) the provisions of Article 26.5, and provided further that the Directors or the members have not (upon request) refused to give specific authorisation pursuant to Article 27 for a particular situation or matter or have otherwise resolved pursuant to Article 27.3 that a particular situation or matter shall no longer be authorised, a Director, notwithstanding his office, shall be authorised:

(a) to enter into, or otherwise be interested in, any transaction or arrangement with the Company or in which the Company is interested, either with regard to his tenure of any office or position in the management, administration or conduct of its business or as seller, buyer or otherwise;

(b) to hold any office or place of profit (except that of auditor) with, or to be employed by or a consultant to or otherwise interested (including by way of the holding of shares or securities convertible into shares) in, the Company, or in any holder of a majority of the voting rights attaching to the issued share capital of the Company or any Associate of any such holder;

(c) to act by himself or by any firm of which he is a partner, director, employee or member in a professional capacity (except as auditor) for the Company, or any holder

of a majority of the voting rights attaching to the issued share capital of the Company or any Associate of any such holder and he or his firm shall be entitled to remuneration for professional services as if he were not a Director of the Company; and

(d) to be a director of any other company in which the Company does not have an interest if that cannot reasonably be regarded as likely to give rise to a conflict of interest at the time of his appointment as a director of the Company or that other company (whichever is the later), and such authorisations shall extend to any direct or indirect interest that conflicts or possibly may conflict with the interests of the Company which may reasonably be expected to arise out of the situations and matters so authorised and which is capable of being authorised at law. No authorisation shall be required pursuant to Article 27 of any such situation or matter authorised by this Article 26.1 and, without limitation, no Director shall, by reason of his holding office as a Director of the Company (or of the fiduciary relationship established by his holding that office), be liable to account to the Company for any remuneration, profit or other benefit received as a result of any interest permitted by this Article and no transaction or arrangement shall be liable to be avoided by reason of any Director having any interest or having received any benefit permitted by this Article.

26.2 The authorisations given pursuant to and the other provisions of Article 26.1 shall extend to and include, without limitation, direct or indirect interests of a Director which arise (or which may potentially arise) due to:

(a) any transaction entered into by the Director or any person who appointed that Director in relation to shares (or securities convertible into shares) debentures or other securities in (a) the Company; or (b) such person or any such Associate of such person;

(b) any guarantee, security or indemnity given or proposed to be given by any Group Company to, or to any person for the benefit of, any person who appointed that Director or, where such person is a company, any Associate of that person;

(c) the recommendation, declaration and payment of any dividend or other distribution by the Company;

(d) any transaction or arrangement proposed, made, terminated or varied between the Company and any person who appointed that Director or any Associate of that person including without limitation transactions or arrangements relating to the sale and supply of goods and services, the borrowing or advancing of money and the use of property and other assets; and

(e) any claim or right arising between the Company and any person who appointed that Director or any Associate of that person.

26.3 It shall be a term and condition of the authorisation given pursuant to Article 26.5 that the Director shall not be entitled to vote or participate in any discussions relating to the exercise, enforcement or pursuance of any claim or right so authorised.

26.4 For the purposes of Articles 26.1 and 26.2 an interest of: (a) a person who is connected with a Director (within the meaning of section 252 of the 2006 Act); and (b) the appointor in relation to any alternate, shall be treated as an interest of the Director or alternate (as appropriate), in each case in addition to any interest which the Director or alternate otherwise has.

26.5 In relation to transactions or arrangements with the Company, the Director shall declare the nature and extent of any interest authorised under Articles 26.1 and 26.2 in any way permitted by the 2006 Act and shall only be required to make such disclosure to the extent

required to do so under the 2006 Act. In relation to other situations of actual or potential conflict of interest, the Director shall declare the nature and extent of his interest at a meeting of the Directors, or as otherwise determined by the Directors, but shall not be required to declare the nature and extent of his interest to the extent that the other Directors are already aware of the interest and its extent.

26.6 Regulation 85 shall not apply.

27. AUTHORISATION OF CONFLICTS OF INTEREST

27.1 Any matter (a "**Relevant Matter**") which would otherwise constitute or give rise to a breach by a Director of his duty under section 175 of the 2006 Act to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts or possibly may conflict with the interests of the Company (including a breach which would arise by virtue of his appointment as a Director) may be authorised by the Directors to the fullest extent permitted by law in accordance with the provisions of Articles 27.2 to 27.4.

27.2 Any Director may propose that a Relevant Matter be authorised by the Directors. Such proposal and any authorisation given by the Directors shall be effected in the same way as any other matter may be proposed to, and resolved upon by, the Directors (or in such other manner as the Directors may approve) in accordance with these Articles, except that no authorisation shall be effective unless the requirements of section 175(6) of the 2006 Act have been complied with. Any authorisation of a matter pursuant to this Article 27 shall, unless it states otherwise, extend to any actual or potential conflict of interest which may reasonably be expected to arise out of the matter so authorised.

27.3 Any authorisation of a matter under Article 27.1 shall be subject to such terms, conditions and limitations as the Directors may specify, whether at the time of giving the authorisation or subsequently. The Directors or the members may terminate or vary (including by imposing new terms, conditions and limitations in relation to) any authorisation given under this Article 27 or under Article 27.1 for the purpose of section 175 of the 2006 Act at any time, but no such termination or variation shall be of retrospective effect. The Director concerned must act in accordance with any terms, conditions or limitations specified by the Directors or the members in accordance with this Article.

27.4 No Director shall, by reason of his office as Director of the Company (or by reason of the fiduciary relationship established by holding that office), be liable to account to the Company for any benefit derived from any Relevant Matter to the extent that the Relevant Matter has been authorised by the Directors in accordance with this Article 27. No transaction or arrangement shall be liable to be avoided by reason of any interest of a Director to the extent that it has been so authorised.

27.5 Notwithstanding the other provisions of this Article 27, the members of the Company shall be entitled to authorise a Relevant Matter (whether or not authorisation has previously been requested from and/or refused by the Directors). The provisions of Articles 27.2 and 27.4 shall apply mutatis mutandis to any authorisation so given by the members save that the word "directors" or "directors or members" in any references to the authorisation being given by the Directors or by the Directors or the members and in any reference to any terms and conditions of authorisation being specified, imposed, varied or terminated by the Directors or by the Directors or the members shall be read only as the word "members". Any authorisation, and the variation or termination of any authorisation by the members under Article 27.3 or this Article shall be by ordinary resolution, save where any greater majority is otherwise required by the 2006 Act or other applicable law.

28. DIRECTORS' INTERESTS: GENERAL

28.1 Where this Article applies, a Director shall be deemed to have the authority, without breaching the general duties he owes to the Company by virtue of sections 171 to 177 of the 2006 Act to (and shall if so requested by the other Directors or the members) take such steps

as may be necessary or desirable for the purpose of managing any conflict of interest to which this Article 28.1 applies, including (without limitation) by:

(a) complying with any procedures laid down from time to time by the Directors for the purpose of managing conflicts of interest generally or any specific procedures approved by the Directors in relation to the situation, matter or interest in question;

(b) excluding himself from attending and voting at board meetings to the extent relating to such situation, matter or interest or from participating in discussions (whether at meetings of the board or otherwise), or receiving documents or information, relating to any such situation, matter or interest (including without limitation, notice of meetings, board papers, minutes or draft minutes and legal advice given to the Company);

(c) arranging for documents or information relating to any such situation, matter or interest to be reviewed by a professional adviser to ascertain the extent to which it might be appropriate for him to have access to such documents or information; and/or

(d) not disclosing to the Company, or not using in relation to the Company's affairs, information which he obtains or has obtained otherwise than through his position as a Director of the Company which relates to a situation, matter or interest and which is confidential to a third party, where to do so would amount to a breach of confidence or breach of duty to the third party.

28.2 Article 28.1 shall apply where a Director has or could have:

(a) a direct or indirect interest that conflicts or possibly may conflict with the interests of the Company and provided that the interest or the existence of the situation or relationship leading to the interest has been authorised pursuant to Article 26.1 or Article 27 and unless otherwise specified by the terms and conditions of such authorisation; and

(b) a direct or indirect interest in a transaction or arrangement with the Company and such interest has been declared to the other Directors to the extent required by the 2006 Act.

28.3 Where a Director obtains or has obtained information, otherwise than through his position as a Director, which is confidential to a third party other than the Company, then provided that the duty of confidentiality does not arise out of a situation in which the Director has or may have a direct or indirect conflict of interest, the Director shall not be required to disclose such information to the Company or use it in relation to the Company's affairs. This Article is without prejudice to the ability of a Director to withhold such information from the Company in accordance with the provisions of Article 28.1.

28.4 Articles 28.1 and 28.3 are without prejudice to any equitable principle or rule of law which may otherwise excuse or release the Director from any requirement to disclose information or use information in relation to the Company's affairs, participate in discussions or receive documents or information.

28.5 For the purposes of Articles 26 to 28 references to a conflict of interest include a conflict of interest and duty and a conflict of duties.

29. WRITTEN RESOLUTIONS

29.1 Any member holding no less than five percent (5%) of the voting rights of the Company may require the Company to circulate a written resolution and if any member does so, the provisions of sections 292(1) to (3) (inclusive) and sections 292(6), 293, 294 and 295 of the 2006 Act shall apply mutatis mutandis to that request as if it were a request made by members pursuant to section 292 of the 2006 Act save that the Company shall be required to

ensure that copies of any written resolution so requested shall be sent or submitted to all members entitled to receive it not later than five (5) days after the date on which the Company received the request (whether or not it has then received an amount to meet its expenses in so doing).

29.2 In the event that any resolution referred to in Article 25.14 is proposed as a written resolution the form of written resolution shall:

(a) provide for every eligible member to be able to indicate whether it is voting for the proposed resolution or against the proposed resolution (and if more than one (1) resolution is proposed, such voting alternatives shall be provided for each resolution); and

(b) require such named individual to hold such authenticated documents on behalf of and as agent for the relevant member and not the Company until the earlier of:

(c) the date on which that named individual has received authenticated documents (indicating either a vote for or against the relevant resolution) from each eligible member whose votes, if cast against the resolution would (pursuant to Article 25.14) carry 50.01% of the votes capable of being cast on that resolution; and

(d) the day before the date on which the written resolution would otherwise lapse in accordance with section 297 of the 2006 Act,

at which time such named individual shall deliver all the authenticated documents held by him as agent of the eligible members to the Company. Any written resolution circulated by the Company shall contain language to effect the requirements of this Article 29.

30. DISQUALIFICATION OF DIRECTORS

In addition to that provided in Regulation 81 of Table A, the office of a Director shall also be vacated if:

(a) he is convicted of a criminal offence (other than a minor motoring offence) and the Directors resolve that his, her or its office be vacated; or

(b) in the case of Directors, other than an Investor Director or a Founder Director, if a majority of his co-Directors serve notice on him in writing, removing him from office.

31. PROCEEDINGS OF DIRECTORS

31.1 The quorum for a Board meeting shall be a majority of the Directors in office and must include at least one Director appointed in accordance with Articles 25.5 to 25.7. If such a quorum is not present within half an hour from the time appointed for the meeting, or if during a meeting such quorum ceases to be present, the meeting shall stand adjourned to the following day at the same time and place. If no Director appointed in accordance with Articles 25.5 to 25.7 is present at any such adjourned meeting within half an hour from the time the adjourned meeting is scheduled to begin, then a quorum shall be deemed to be present providing a majority of the Directors in office are present and the adjourned meeting shall proceed.

31.2 In its application to the Company, Regulation 88 of Table A shall be modified by the deletion of the second and third sentences.

31.3 In its application to the Company Regulation 89 of Table A shall be modified:

(a) by the deletion of the words "*may be fixed by the Directors and unless so fixed at any other number*" in the first sentence; and

(b) by the addition of the following as the final sentence: "*In the event that a meeting of the Directors is attended by a Director who is acting as alternate for one (1) or more other Directors, the Director or Directors for whom he is the alternate shall not be counted in the quorum for the purposes of the meeting*".

31.4 Any Director who participates in the proceedings of a meeting by means of a communication device (including a telephone) which allows all the other Directors present at that meeting (whether in person or by alternate or by means of that type of communication device) to hear at all times that Director and that Director to hear at all times all other Directors present at the meeting (whether in person or by alternate or by means of that type of communication device) shall be deemed to be present at the meeting and shall be counted when reckoning a quorum. A meeting held by these means shall be deemed to take place where the largest group of participators in number is assembled. In the absence of a majority the location of the chairman shall be deemed to be the place of the meeting.

31.5 A Director may vote at a meeting of the Directors, and form part of a quorum present at that meeting, in relation to any matter in which he has, directly or indirectly, an interest or duty which conflicts or which may conflict with the interests of the Company, provided that he has previously disclosed the nature of such duty or interest to the Directors. The provisions of Regulation 86 of Table A shall be taken to apply equally to any disclosure to be made under the provisions of this Article.

31.6 Questions arising at any meeting of the Directors shall be decided by a majority of votes. In the case of any equality of votes, the chairman shall not have a second or casting vote.

31.7 Decisions at any meeting of the Directors shall be decided by a majority of votes, including at least one of the Directors appointed pursuant to Articles 25.1 to 25.4, at least one of the Directors appointed pursuant to Articles 25.5 to 25.7 and at least one of the Directors appointed pursuant to Articles 25.8 to 25.10.

32. EXECUTION OF DOCUMENTS

In its application to the Company Regulation 101 of Table A shall be modified by the addition of the following sentence:

"*Any instrument expressed to be executed by the Company and signed by two (2) Directors, by one Director and the Secretary, by the authority of the Directors, or the 2006 Act of a committee authorised by the Directors or as otherwise permitted under the 2006 Act shall (to the extent permitted by the 2006 Act) have effect as if executed under seal*."

33. DIVIDENDS

In Regulation 103 of Table A the words from "*If the share capital is divided*" to the end of the third sentence of the Regulation shall be deleted.

34. NOTICES

34.1 Any notice shall be in writing and shall be conclusively deemed to have been duly given:

(a) when hand delivered to the relevant party;

(b) when received when sent by facsimile, e-mail or any other form of electronic communication at the relevant address (and as confirmed by the recipient);

(c) two (2) Business Days after dispatch if sent to an address in the United Kingdom by post;

(d) five (5) Business Days after dispatch if sent by reputable international overnight courier addressed to the relevant party provided that delivery in at least five (5) Business Days was guaranteed at the time of sending and the sending Party receives a confirmation of delivery from the courier service provider; or

(e) by airmail (registered or certified) fifteen (15) Business Days after sending.

34.2 In proving service of a notice it shall be sufficient to prove that personal delivery was made, or that the relevant notice or other written communication was properly addressed stamped and posted or in the case of a facsimile, e-mail or other form of electronic communication evidence that the relevant communication was properly sent.

34.3 Regulation 115 of Table A shall be deleted.

35. INDEMNITY AND INSURANCE

35.1 Subject to the provisions of and so far as may be consistent with the 2006 Act the Directors may exercise all the powers of the Company to indemnify any person who is, or was at any time, a Director of the Company or of any of its associated companies against all liabilities incurred by or attaching to him in connection with his duties, powers or office in relation to any such company of which he is or was a Director, to the fullest extent permitted by law.

35.2 Regulation 118 shall not apply.

35.3 Without prejudice to Article 35.1 the Directors may exercise all the powers of the Company to purchase and maintain insurance for or for the benefit of any person who is or was at any time:

(a) a Director, alternate director or other officer of any Relevant Company (as defined in Article 35.4 below); or

(b) a trustee of any pension fund or retirement, death or disability scheme for the benefit of any employee of any Relevant Company or employees' share scheme in which employees of any Relevant Company are interested,

including (without limitation) insurance against any liability within Article 35.1 attaching to him in relation to any Relevant Company, or any such pension fund, retirement or other scheme or employees' share scheme.

35.4 For these purposes "**Relevant Company**" shall mean the Company or any other undertaking which is:

(a) the holding company of the Company;

(b) a Subsidiary of the Company or of such holding company; or

(c) a company in which the Company has an interest (whether direct or indirect).

36. DATA PROTECTION

Each of the shareholders and Directors of the Company (from time to time) consent to the processing of their personal data by the Company, its shareholders and Directors (each a "**Recipient**") for the purpose of due diligence exercises, compliance with applicable laws, regulations and procedures and the exchange of information among themselves. A Recipient may process the personal data either electronically or manually. The personal data which

may be processed under this Article shall include any information which may have a bearing on the prudence or commercial merits of investing, or disposing of any shares (or other investment or security) in the Company. Other than as required by law, court order or other regulatory authority, that personal data may not be disclosed by a Recipient or any other person except to a Member of the Same Group or a Member of the Same Fund Group (the "**Recipient Group Companies**") and to employees, directors and professional advisers of that Recipient or the Recipient Group Companies and funds managed by any of the Recipient Group Companies. Each of the Company's shareholders and Directors (from time to time) consent to the transfer of relevant personal data to persons acting on behalf of the Recipient and to the offices of any Recipient both within and outside the European Economic Area for the purposes stated above, where it is necessary or desirable to do so.

Exhibit 3.2

DATED 2019

The Companies Act 2006
Public Company Limited by shares

ARTICLES OF ASSOCIATION

of

BICYCLE THERAPEUTICS PLC

TABLE OF CONTENTS

Company number: 11036004

NEW

ARTICLES OF ASSOCIATION

of

BICYCLE THERAPEUTICS PLC

(the "**Company**")

1 **Defined terms**

1.1 No regulations or articles set out in any statute, or in any statutory instrument or other subordinate legislation made under any statute, concerning companies (including the regulations in the Companies (Model Articles) Regulations 2008 (SI 2008/3229)) shall apply as the articles of the Company. The following shall be the articles of association of the Company.

2 **Interpretation**

2.1 In these Articles, the following words and expressions shall have the meanings set out below:

"**Act**" means the Companies Act 2006

"**address**" includes any number or address used for the purposes of sending or receiving documents or information by electronic means

"**Articles**" means these articles of association as altered from time to time and Article shall be construed accordingly

"**Board**" means the board of Directors for the time being of the Company or the Directors present or deemed to be present at a duly convened quorate meeting of the Directors

"**certificated shares**" means a share which is not an uncertificated share and references in these Articles to a share being held in certificated form shall be construed accordingly

"**clear days**" in relation to a period of notice, means that period excluding the day when the notice is served or deemed to be served and the day for which it is given or on which it is to take effect

"**Companies Acts**" means the Act, the Companies Act 1985 and, where the context requires, every other statute from time to time in force concerning companies and affecting the Company

"**Director**" means a director for the time being of the Company

"**electronic facility**" means, without limitation, website addresses and conference call systems, and any device, system, procedure, method or other facility whatsoever providing an electronic means of attendance at or participation in (or both attendance at and participation in) a general meeting determined by the Board pursuant to Article 45.

"FSMA" means the Financial Services and Markets Act 2000

"**electronic form**" has the meaning given to it in section 1168 of the Act

"**electronic means**" has the meaning given to it in section 1168 of the Act

"**Listing**" means the listing of the Company's Ordinary Shares (in the form of American depositary shares) on NASDAQ

"**member**" means a member of the Company, or where the context requires, a member of the Board or of any committee

"**NASDAQ**" means The NASDAQ Stock Market LLC

"**NASDAQ Rules**" means the rules of NASDAQ

"**Office**" means the registered office from time to time of the Company

"**Operator**" means Euroclear UK and Ireland Limited or such other person as may for the time being be approved by HM Treasury as Operator under the uncertificated securities rules

"**Ordinary Shares**" has the meaning given to it in Article 4

"**paid up**" means paid up or credited as paid up

"**participating class**" means a class of shares title to which is permitted by the Operator to be transferred by means of a relevant system.

"**Register**" means the register of members of the Company to be maintained under the Act or as the case may be any overseas branch register maintained under Article 117

"**relevant system**" means a computer-based system which allows units of securities without written instruments to be transferred and endorsed pursuant to the uncertificated securities rules

"**Seal**" means the common seal of the Company or, where the context allows, any official seal kept by the Company under section 50 of the Act

"**Secretary**" means the secretary of Company for the time being

"**uncertificated securities rules**" means any provision of the Companies Acts relating to the holding, evidencing of title to, or transfer of uncertificated shares and any legislation, rules or other arrangements made under or by virtue of such provision (including the Uncertificated Securities Regulations 2001 as amended or replaced from time to time and any subordinate legislation or rules made under them for them time being in force)

"**uncertificated share**" means a share of a class which is at the relevant time a participating class, title to which is recorded on the Register as being held in uncertificated form and references in these Articles to a share being held in uncertificated form shall be construed accordingly

2.2 Headings are used for convenience only and shall not affect the construction or interpretation of these Articles.

2.3 A **person** includes a natural person, a corporate or an unincorporated body (whether or not having separate legal personality).

2.4 Words in the singular shall include the plural and vice versa.

2.5 A reference to one gender shall include a reference to the other gender.

2.6 A reference to a statute or statutory provision is a reference to it as it is in force for the time being, taking account of any amendment, extension, or re-enactment and includes any subordinate legislation for the time being in force made under it.

2.7 Any words or expressions defined in the Companies Acts in force when these Articles or any part of these Articles are adopted shall (if not inconsistent with the subject or context in which they appear) have the same meaning in these Articles or that part, save that the word **company** shall include any company, corporation or other body corporate, wherever and however incorporated or established.

2.8 A reference to a document **being signed** or to **signature** includes references to its being executed under hand or under seal or by any other method and, in the case of a communication in electronic form, such references are to its being authenticated as specified by the Companies Acts.

2.9 A reference to **writing** or **written** includes references to any method of representing or reproducing words in a legible and non-transitory form whether sent or supplied in electronic form or otherwise.

2.10 A reference to documents or information **being sent or supplied by or to** a company (including the Company) shall be construed in accordance with section 1148(3) of the Act.

2.11 A reference to a **meeting**:

(a) shall mean a meeting convened and held in any manner permitted by these Articles, including a general meeting at which some (but not all) of those persons entitled to be present, attend and participate by means of electronic facility or facilities, and such persons shall be deemed to be present at that meeting for all purposes of the Act and these Articles, and attend, participate, attending, participating, attendance and participation shall be construed accordingly; and

(b) shall not be taken as requiring more than one person to be present if any quorum requirement can be satisfied by one person.

2.12 If any Article (or part thereof) is or becomes inconsistent with any laws or regulations of any country to which affairs of the Company are subject such laws or regulations shall prevail and the relevant Article (or part thereof) shall be construed accordingly.

2.13 References to a person's participation in the business of a general meeting include without limitation and as relevant the right (including, in the case of a corporation, through a duly appointed representative) to speak, vote, be represented by a proxy and have access in hard copy or electronic form to all documents which are required by the Companies Acts or these Articles to be made available at the meeting, and participate and participating in the business of a general meeting shall be construed accordingly.

2.14 Nothing in these Articles precludes the holding and conducting of a general meeting in such a way that persons who are not present together at the same place or places may by electronic means attend and participate in it.

3 **Form of Resolution**

Subject to the Companies Acts, where anything can be done by passing an ordinary resolution, this can also be done by passing a special resolution.

4 **Capital**

The capital of the Company is divided into an unlimited number of ordinary shares of £0.01 each ("**Ordinary Shares**") conferring on the holders the rights and being subject to the restrictions set out in this Article 10.

5 **Limited Liability**

The liability of the members of the Company is limited to the amount, if any, unpaid on the shares in the Company held by them.

6 **Change of Name**

The Company may change its name by resolution of the Board.

7 **Power to Attach Rights to Shares**

Subject to the Companies Acts and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the Company may by ordinary resolution determine, or if no ordinary resolution has been passed or so far as the resolution does not make specific provision, as the Board may determine.

8 **Allotment of Shares and Pre-Emption**

8.1 Subject to the Companies Acts, these Articles and to any relevant authority of the Company in general meeting required by the Act, the Board may offer, allot (with or without conferring rights of renunciation), grant options over or otherwise deal with or dispose of shares or grant rights to subscribe for or convert any security into shares to such persons, at such times and upon such terms as the Board may decide. No share may be issued at a discount.

8.2 The Board may, at any time after the allotment of any share but before any person has been entered in the Register, recognise a renunciation by the allottee in favour of some other person and accord to the allottee of a share a right to effect such renunciation and/or allow the rights to be represented to be one or more participating securities, in each case upon and subject to such terms and conditions as the Board may think fit to impose.

8.3 Under and in accordance with section 551 of the Act, the Directors shall be generally and unconditionally authorised to exercise for each prescribed period all the powers of the Company to allot shares up to an aggregate nominal amount equal to the Section 551 Amount (as defined below).

8.4 Under and within the terms of the said authority or otherwise in accordance with section 570 of the Act, the Directors shall be empowered during each prescribed period to allot equity securities (as defined by the Act) wholly for cash:

(a) in connection with a rights issue; and

(b) otherwise than in connection with a rights issue up to an aggregate nominal amount equal to the Section 561 Amount (as defined below).

8.5 During each prescribed period the Company and its Directors by such authority and power may make offers or agreements which would or might require equity securities or other securities to be allotted after the expiry of such period.

8.6 For the purposes of this Article 8:

(a) **rights issue** means an offer of equity securities (as defined by the Act) open for acceptance for a period fixed by the Board to holders of equity securities on the Register on a fixed record date in proportion to their respective holdings of such securities or in accordance with the rights attached to them but subject to such exclusions or other arrangements as the Board may deem necessary or expedient with regard to treasury shares, fractional entitlements or legal or practical problems under the laws of any territory or under the requirements of any recognised regulatory body or stock exchange in any territory;

(b) **prescribed period** means any period (not exceeding five years on any occasion) for which the authority, in the case of Article 8.3, is conferred or renewed by ordinary or special resolution stating the Section 551 Amount and in the case of Article 8.4 is conferred or renewed by special resolution stating the Section 561 Amount;

(c) **Section 551 Amount** means for any prescribed period, the amount stated in the relevant ordinary or special resolution;

(d) **Section 561 Amount** means for any prescribed period, the amount stated in the relevant special resolution; and

(e) the nominal amount of any securities shall be taken to be, in the case of rights to subscribe for or to convert any securities into shares of the Company, the nominal amount of such shares which may be allotted pursuant to such rights.

9 **Redeemable Shares**

Subject to the Companies Acts and to any rights attaching to existing shares, any share may be issued which can be redeemed or is liable to be redeemed at the option of the Company or the holder. The Board may determine the terms, conditions and manner of redemption of any redeemable shares which are issued. Such terms and conditions shall apply to the relevant shares as if the same were set out in these Articles.

10 **Shareholder Rights**

10.1 The Ordinary Shares shall rank pari passu as a single class.

10.2 In the event of the liquidation, dissolution or winding up of the Company, the assets of the Company available for distribution to members shall be distributed amongst all holders of the Ordinary Shares in proportion to the number of shares held irrespective of the amount paid or credited as paid on any share.

10.3 Any:

(a) consolidation or merger of the Company with or into another entity or entities (whether or not the Company is the surviving entity) as a result of which the holders of the Company's outstanding shares possessing the voting power (under ordinary circumstances) to elect a majority of the Board immediately prior to such sale or issue cease to own the Company's outstanding shares possessing the voting power (under ordinary circumstances) to elect a majority of the Board;

(b) sale or transfer by the Company of all or substantially all of its assets (determined either for the Company alone or together with its subsidiaries on a consolidated basis); or

(c) sale, transfer or issuance or series of sales, transfers and/or issues of shares by the Company or the holders thereof, as a result of which the holders of the Company's outstanding shares possessing the voting power (under ordinary circumstances) to

elect a majority of the Board immediately prior to such sale or issue cease to own the Company's outstanding shares possessing the voting power (under ordinary circumstances) to elect a majority of the Board,

shall be deemed to be a liquidation, dissolution and winding up of the Company for purposes of Article 10.2 (unless the Board determine otherwise), and the holders of the Ordinary Shares shall be entitled to receive from the Company the amounts payable with respect to the Ordinary Shares on a liquidation, dissolution or winding up of the Company under Article 10.2 in cancellation of their Ordinary Shares upon the completion of any such transaction.

10.4 At a general meeting of the Company and at any separate class meeting of the holders of Ordinary Shares, where a holder of Ordinary Shares is entitled to vote, such holder is entitled to one vote for each Ordinary Share held.

10.5 A holder of Ordinary Shares is entitled to receive notice of any general meeting of the Company (and notice of any separate class meeting of the holders of Ordinary Shares) and a copy of every report, accounts, circular or other document sent out by the Company to members.

11 **Pari Passu Issues**

If new shares are created or issued which rank equally with any other existing shares, the rights of the existing shares will not be regarded as changed or abrogated unless the terms of the existing shares expressly say otherwise.

12 **Variation of Rights**

12.1 Subject to the Companies Acts, the rights attached to any class of shares can be varied or abrogated either with the consent in writing of the holders of not less than three-quarters in nominal value of the issued share of that class (excluding any shares of that class held as treasury shares) or with the authority of a special resolution passed at a separate meeting of the holders of the relevant class of shares known as a class meeting.

12.2 The provisions of this Article will apply to any variation or abrogation of rights of shares forming part of a class. Each part of the class which is being treated differently is treated as a separate class in applying this Article.

12.3 All the provisions in these Articles as to general meetings shall apply, with any necessary modifications, to every class meeting except that:

(a) the quorum at every such meeting shall not be less than two persons holding or representing by proxy at least one-third of the nominal amount paid up on the issued shares of the class) (excluding any shares of that class held as treasury shares); and

(b) if at any adjourned meeting of such holders such quorum as set out above is not present, at least one person holding shares of the class who is present in person or by proxy shall be a quorum.

12.4 The Board may convene a class meeting whenever it thinks fit and whether or not the business to be transacted involves a variation or abrogation of class rights.

13 **Payment of Commission**

The Company may in connection with the issue of any shares or the sale for cash of treasury shares exercise all powers of paying commission and brokerage conferred or permitted by the Companies Acts. Any such commission or brokerage may be satisfied by the payment of

cash or by the allotment of fully or partly paid shares or other securities or the grant of an option to call for an allotment of shares or any combination of such methods.

14 **Trusts Not Recognised**

Except as otherwise expressly provided by these Articles, required by law or as ordered by a court of competent jurisdiction, the Company shall not recognise any person as holding any share on any trust, and the Company shall not be bound by or required in any way to recognise (even when having notice of it) any equitable, contingent, future, partial or other claim to or interest in any share other than an absolute right of the holder of the whole of the share.

15 **Uncertificated Shares**

15.1 Under and subject to the uncertificated securities rules, the Board may permit title to shares of any class to be evidenced otherwise than by certificate and title to shares of such a class to be transferred by means of a relevant system and may make arrangements for a class of shares (if all shares of that class are in all respects identical) to become a participating class. Title to shares of a particular class may only be evidenced otherwise than by a certificate where that class of shares is at the relevant time a participating class. The Board may also, subject to compliance with the uncertificated securities rules, determine at any time that title to any class of shares may from a date specified by the Board no longer be evidenced otherwise than by a certificate or that title to such a class shall cease to be transferred by means of any particular relevant system.

15.2 In relation to a class of shares which is a participating class and for so long as it remains a participating class, no provision of these Articles shall apply or have effect to the extent that it is inconsistent in any respect with:

(a) the holding of shares of that class in uncertificated form;

(b) the transfer of title to shares of that class by means of a relevant system; or

(c) any provision of the uncertificated securities rules,

and, without prejudice to the generality of this Article, no provision of these Articles shall apply or have effect to the extent that it is in any respect inconsistent with the maintenance, keeping or entering up by the Operator, so long as that is permitted or required by the uncertificated securities rules, of an Operator register of securities in respect of that class of shares in uncertificated form.

15.3 Ordinary Shares of a class which is at the relevant time a participating class may be changed from uncertificated to certificated form, and from certificated to uncertificated form, in accordance with and subject as provided in the uncertificated securities rules.

15.4 If, under these Articles or the Companies Acts, the Company is entitled to sell, transfer or otherwise dispose of, forfeit, re-allot, accept the surrender of or otherwise enforce a lien over an uncertificated share, then, subject to these Articles and the Companies Acts, such entitlement shall include the right of the Board to:

(a) require the holder of the uncertificated share by notice in writing to change that share from uncertificated to certificated form within such period as may be specified in the notice and keep it as a certificated share for as long as the Board requires;

(b) appoint any person to take such other steps, by instruction given by means of a relevant system or otherwise, in the name of the holder of such share as may be required to effect the transfer of such share and such steps shall be as effective as if they had been taken by the registered holder of that share; and

(c) take such other action that the Board considers appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of that share or otherwise to enforce a lien in respect of that share.

15.5 Unless the Board determines otherwise, shares which a member holds in uncertificated form shall be treated as separate holdings from any shares which that member holds in certificated form but a class of shares shall not be treated as two classes simply because some shares of that class are held in certificated form and others in uncertificated form.

15.6 Unless the Board determines otherwise or the uncertificated securities rules require otherwise, any shares issued or created out of or in respect of any uncertificated shares shall be uncertificated shares and any shares issued or created out of or in respect of any certificated shares shall be certificated shares.

15.7 The Company shall be entitled to assume that the entries on any record of securities maintained by it in accordance with the uncertificated securities rules and regularly reconciled with the relevant Operator register of securities are a complete and accurate reproduction of the particulars entered in the Operator register of securities and shall accordingly not be liable in respect of any act or thing done or omitted to be done by or on behalf of the Company in reliance on such assumption. Any provision of these Articles which requires or envisages that action will be taken in reliance on information contained in the Register shall be construed to permit that action to be taken in reliance on information contained in any relevant record of securities (as so maintained and reconciled).

16 **Share Certificates**

16.1 Every person (except a person to whom the Company is not by law required to issue a certificate) whose name is entered in the Register as a holder of any certificated shares shall be entitled, without charge, to receive within the time limits prescribed by the Companies Acts (unless the terms of issue prescribe otherwise) one certificate for all of the shares of that class registered in his name.

16.2 The Company shall not be bound to issue more than one certificate in respect of shares held jointly by two or more persons. Delivery of a certificate to the person first named in the Register shall be sufficient delivery to all joint holders.

16.3 Where a member has transferred part only of the shares comprised in a certificate, the member shall be entitled without charge to a certificate for the balance of such shares to the extent that the balance is to be held in certificated form. Where a member receives more shares of any class, the member shall be entitled without charge to a certificate for the extra shares of that class to the extent that the balance is to be held in certificated form.

16.4 A share certificate may be issued under Seal (by affixing the Seal to or printing the Seal or a representation of it on the certificate) or signed by at least two Directors or by at least one Director and the Secretary. Such certificate shall specify the number and class of the shares in respect of which it is issued and the amount or respective amounts paid up on it. The Board may be resolution decide, either generally or in any particular case or cases, that any signatures on any share certificates need not be autographic but may be applied to the certificates by some mechanical or other means or may be printed on them or that the certificates need not be signed by any person.

16.5 Every share certificate sent in accordance with these Articles will be sent at the risk of the member or other person entitled to the certificate. The Company will not be responsible for any share certificate lost or delayed in the course of delivery.

17 **Replacement Certificates**

17.1 Any two or more certificates representing shares of any one class held by any member may at the request of the member be cancelled and a single new certificate for such shares issued in lieu without charge on surrender of the original certificates for cancellation.

17.2 Any certificate representing shares of any one class held by any member may at the request of the member be cancelled and two or more certificates for such shares may be issued instead.

17.3 If a share certificate is defaced, worn out or said to be stolen, lost or destroyed, it may be replaced on such terms as to evidence and indemnity as the Board may decide and, where it is defaced or worn out, after delivery of the old certificate to the Company.

17.4 The Board may require the payment of any exceptional out-of-pocket expenses of the Company incurred in connection with the issue of any certificates under this Article. In the case of shares held jointly by several persons, any such request as is mentioned in this Article may be made by any one of the joint holders.

18 **Lien on Shares not Fully Paid**

The Company shall have a first and paramount lien on every share, not being a fully paid share, for all amounts payable to the Company (whether presently or not) in respect of that share. The Company's lien over a share takes priority over any third party's interest in that share, and extends to any dividend or other money payable by the Company in respect of that share (and, if the lien is enforced and the share is sold by the Company, the proceeds of sale of that share). The Board may at any time, either generally or in any particular case, waive any lien that has arisen or declare any share to be wholly or in part exempt from the provisions of this Article.

19 **Enforcement of Lien by Sale**

The Company may sell, in such manner as the Board may decide, any share over which the Company has a lien if a sum in respect of which the lien exists is presently payable and is not paid within 14 clear days after a notice has been served on the holder of the share or the person who is entitled by transmission to the share, demanding payment and stating that if the notice is not complied with the share may be sold. For giving effect to the sale, in the case of a certificated share, the Board may authorise some person to sign an instrument of transfer of the share sold to, or in accordance with the directions, of the buyer. In the case of an uncertificated share, the Board may require the Operator to convert the share into certificated form and after such conversion, authorise any person to sign the instrument of transfer of the share to affect the sale of the share. The buyer shall not be bound to see to the application of the purchase money, nor shall the buyer's title to the share be affected by any irregularity or invalidity in the proceedings in reference to the sale.

20 **Application of Proceeds of Sale**

The net proceeds of any sale of shares subject to any lien, after payment of the costs, shall be applied:

(a) first, in or towards satisfaction of so much of the amount due to the Company or of the liability or engagement (as the case may be) as is presently payable or is liable to be presently fulfilled or discharged; and

(b) second, any residue shall be paid to the person who was entitled to the share at the time of the sale but only after the certificate for the shares sold has been surrendered to the company for cancellation, or an indemnity in a form reasonably satisfactory to the directors has been given for any lost certificates, and subject to a

like lien for debts or liabilities not presently payable as existed on the share prior to the sale.

21 **Calls**

21.1 Subject to these Articles and the terms on which the shares are allotted, the Board may from time to time make calls on the members in respect of any monies unpaid on their shares (whether in respect of nominal value or premium) and not payable on a date fixed by or in accordance with the terms of issue.

21.2 Each member shall (subject to the Company serving upon him at least 14 clear days' notice specifying when and where payment is to be made and whether or not by instalments) pay to the Company as required by the notice the amount called on such member's shares.

21.3 A call shall be deemed to have been made at the time when the resolution of the Board authorising the call was passed.

21.4 A call may be revoked or postponed, in whole or in part, as the Board may decide.

21.5 Liability to pay a call is not extinguished or transferred by transferring the shares in respect of which the call is required to be paid.

22 **Liability of Joint Holders**

The joint holders of a share shall be jointly and severally liable to pay all calls in respect of the share.

23 **Interest on Calls**

If a call remains unpaid after it has become due and payable, the person from whom it is due and payable shall pay all expenses that have been incurred by the Company by reason of such non-payment together with interest on the amount unpaid from the day it is due and payable to the time of actual payment at such rate (not exceeding the Bank of England base rate by more than five percentage points) as the Board may decide. The Board may waive payment of the interest or the expenses in whole or in part.

24 **Power to Differentiate**

On or before the issue of shares, the Board may decide that allottees or holders of shares can be called on to pay different amounts or that they can be called on at different times.

25 **Payment of Calls in Advance**

The Board may, if it thinks fit, receive from any member willing to advance the same, all or any part of the monies uncalled and unpaid on the shares held by him. Such payment in advance of calls shall, to the extent of the payment, extinguish the liability on the shares on which it is made. The Company may pay interest on the money paid in advance, or so much of it as exceeds the amount for the time being called upon the shares in respect of which such advance has been made, at such rate as the Board may decide. The Board may at any time repay the amount so advanced by giving at least three months' notice in writing to such member of its intention to do so, unless before the expiration of such notice the amount so advanced shall have been called up on the shares in respect of which it was advanced.

26 **Notice if Call or Instalment Not Paid**

If any member fails to pay the whole of any call (or any instalment of any call) by the date when payment is due, the Board may at any time give notice in writing to such member (or to

any person entitled to the shares by transmission), requiring payment of the amount unpaid (and any accrued interest and any expenses incurred by the Company by reason of such non-payment) by a date not less than 14 clear days from the date of the notice. The notice shall name the place where the payment is to be made and state that, if the notice is not complied with, the shares in respect of which such call was made will be liable to be forfeited.

27 **Forfeiture for Non-Compliance**

If the notice referred to in Article 26 is not complied with, any share for which it was given may be forfeited, by resolution of the Board to that effect, at any time before the payment required by the notice has been made. Such forfeiture shall include all dividends declared or other monies payable in respect of the forfeited shares and not paid before the forfeiture.

28 **Notice After Forfeiture**

When any share has been forfeited, notice of the forfeiture shall be served on the holder of the share or the person entitled to such share by transmission (as the case may be) before forfeiture. An entry of such notice having been given and of the forfeiture and the date of forfeiture shall immediately be made in the Register in respect of such share. However, no forfeiture shall be invalidated by any omission to give such notice or to make such entry in the Register.

29 **Forfeiture May Be Annulled**

The Board may annul the forfeiture of a share, at any time before any forfeited share has been cancelled or sold, re-allotted or otherwise disposed of, on the terms that payment shall be made of all calls and interest due on it and all expenses incurred in respect of the share and on such further terms (if any) as the Board shall see fit.

30 **Surrender**

The Board may accept the surrender of any share liable to be forfeited and, in any event, references in these Articles to forfeiture shall include surrender.

31 **Sale of Forfeited Shares**

31.1 A forfeited share shall become the property of the Company.

31.2 Subject to the Companies Acts, any such share may be sold, re-allotted or otherwise disposed of, on such terms and in such manner as the Board thinks fit.

31.3 The Board may, for the purposes of the disposal, authorise some person to transfer the share in question and may enter the name of the transferee in respect of the transferred share in the Register even if no share certificate is lodged and may issue a new certificate to the transferee. An instrument of transfer executed by that person shall be as effective as if it had been executed by the holder of or the person entitled by transmission to, the share. The Company may receive the consideration (if any) given for the share on its disposal.

32 **Effect of Forfeiture**

A member whose shares have been forfeited shall cease to be a member in respect of such forfeited shares and shall surrender the certificate for such shares to the Company for cancellation. Such member shall remain liable to pay to the Company all sums which at the date of forfeiture were presently payable by him to the Company in respect of such shares with interest (not exceeding the Bank of England base rate by two percentage points) from the date of the forfeiture to the date of payment. The Directors may waive payment of interest wholly or in part and may enforce payment, without any reduction or allowance for the value of the shares at the time of forfeiture or for any consideration received on their disposal.

33 **Evidence of Forfeiture**

A statutory declaration by a Director or the Secretary that a share has been forfeited on a specified date shall be conclusive evidence of the facts stated in it as against all persons claiming to be entitled to the share. The declaration shall (subject to the execution of an instrument of transfer if necessary) constitute a good title to the share. The person to whom the share is transferred or sold shall not be bound to see to the application of the purchase money or other consideration (if any), nor shall his title to the share be affected by any act, omission or irregularity relating to or connected with the proceedings in reference to the forfeiture or disposal of the share.

34 **Form of Transfer**

34.1 Subject to these Articles:

(a) each member may transfer all or any of his shares which are in certificated form by instrument of transfer in writing in any usual form or in any form approved by the Board. Such instrument shall be executed by or on behalf of the transferor and (in the case of a transfer of a share which is not fully paid up) by or on behalf of the transferee. All instruments of transfer, when registered, may be retained by the Company.

(b) each member may transfer all or any of his shares which are in uncertificated form by means of a relevant system in such manner provided for, and subject as provided in, the uncertificated securities rules. No provision of these Articles shall apply in respect of an uncertificated share to the extent that it requires or contemplates the effecting of a transfer by an instrument in writing or the production of a certificate for the share to be transferred.

34.2 The transferor of a share shall be deemed to remain the holder of the share concerned until the name of the transferee is entered in the Register in respect of it.

35 **Right to Refuse Registration of Transfer**

35.1 The Board may, in its absolute discretion, refuse to register any transfer of a share in certificated form (or renunciation of a renounceable letter of allotment) unless:

(a) it is for a share which is fully paid up;

(b) it is for a share upon which the Company has no lien;

(c) it is only for one class of share;

(d) it is in favour of a single transferee or no more than four joint transferees;

(e) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the Board to be exempt from stamp duty (if this is required); and

(f) is delivered for registration to the Office (or such other place as the Board may determine), accompanied (except in the case of a transfer by a person to whom the Company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the Board may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

35.2 The Board shall not refuse to register any transfer or renunciation of partly paid shares which are admitted to, or for which certificated or uncertificated depositary instruments over such shares are admitted to, NASDAQ on the grounds that they are partly paid shares in circumstances where such refusal would prevent dealings in such shares from taking place on an open and proper basis.

35.3 Transfers of shares will not be registered in the circumstances referred to in Article 72.

35.4 The Board may refuse to register a transfer of uncertificated shares in any circumstances that are allowed or required by the uncertificated securities rules and the relevant system.

36 **Notice of Refusal to Register a Transfer**

If the Board refuses to register a transfer of a share it shall notify the transferee of the refusal and the reasons for it within two months after the date on which the transfer was lodged with the Company or the instructions to the relevant system received. Any instrument of transfer which the Board refuses to register shall be returned to the person depositing it (except if there is suspected or actual fraud). All instruments of transfer which are registered may be retained by the Company.

37 **No Fees on Registration**

No fee shall be charged for registration of a transfer or other document or instruction relating to or affecting the title to any share or for making any other entry in the Register.

38 **Other Powers in Relation to Transfers**

Nothing in these Articles shall prevent the Board:

(a) from recognising a renunciation of the allotment of any share by the allottee in favour of another person; or

(b) (if empowered to do so by these Articles) from authorising any person to execute an instrument of transfer of a share and from authorising any person to transfer that share in accordance with any procedures implemented under Article 19.

39 **Transmission of Shares on Death**

If a member dies, the survivors or survivor (where the member was a joint holder), and his executors or administrators (where the member was a sole or the only survivor of joint holders), shall be the only persons recognised by the Company as having any title to his shares. Nothing in these Articles shall release the estate of a deceased member from any liability for any share which has been solely or jointly held by such member.

40 **Election of Person Entitled By Transmission**

40.1 Any person becoming entitled to a share because of the death or bankruptcy of a member, or otherwise by operation of law, may (on such evidence as to his title being produced as the Board may require) elect either to become registered as a member or to have some person nominated by him registered as a member. If such person elects to become registered himself, he shall notify the Company to that effect. If such person elects to have some other person registered, he shall execute an instrument of transfer of such share to that person. All the provisions of these Articles relating to the transfer of shares shall apply to the notice or instrument of transfer (as the case may be) as if it were an instrument of transfer executed by the member and his death, bankruptcy or other event had not occurred. Where the entitlement of a person to a share because of the death or bankruptcy of a member or otherwise by operation of law is proved to the satisfaction of the Board, the Board shall within 30 days after proof cause the entitlement of that person to be noted in the Register.

40.2 A person entitled by transmission to a share in uncertificated form who elects to have some other person registered shall either:

(a) procure that instructions are given by means of the relevant system to effect transfer of such uncertificated share to that person; or

(b) change the uncertificated share to certificated form and execute an instrument of transfer of that certificated share to that person.

41 **Rights on Transmission**

Where a person becomes entitled to a share because of the death or bankruptcy of any member, or otherwise by operation of law, the rights of the holder in relation to such share shall cease. However, the person so entitled may give a good discharge for any dividends and other monies payable in respect of it and shall have the same rights to which he would be entitled if he were the holder of the share, except that he shall not be entitled to receive notice of, or to attend or vote at, any meeting of the Company or any separate meeting of the holders of any class of shares of the Company before he is registered as the holder of the share. The Board may at any time give notice requiring any such person to elect either to be registered himself or to transfer the share. If the notice is not complied with within 30 days, the Board may withhold payment of all dividends and the other monies payable in respect of such share until the requirements of the notice have been complied with.

42 **Destruction of Documents**

42.1 The Company may destroy any:

(a) instrument of transfer, after six years from the date on which it is registered;

(b) dividend mandate or any variation or cancellation of a dividend mandate or any notification of change of name or address, after two years from the date on which it is recorded;

(c) share certificate, after one year from the date on which it is cancelled;

(d) instrument of proxy which has been used for the purpose of a poll at any time after one year has elapsed from the date of use;

(e) instrument of proxy which has not been used for the purpose of a poll at any time after a period of one month has elapsed from the end of the meeting to which the instrument of proxy relates; or

(f) other document for which any entry in the Register is made, after six years from the date on which an entry was first made in the Register in respect of it,

provided that the Company may destroy any such type of document at a date earlier than that authorised by this Article if a copy of such document is made and retained (whether electronically, by microfilm, by digital imaging or by other similar means) until the expiration of the period applicable to the destruction of the original of such document.

42.2 It shall be conclusively presumed in favour of the Company that every:

(a) entry in the Register purporting to have been made on the basis of a document so destroyed was duly and properly made;

(b) instrument of transfer so destroyed was duly registered;

(c) share certificate so destroyed was duly cancelled; and

(d) other document so destroyed had been properly dealt with under its terms and was valid and effective according to the particulars in the records of the Company.

42.3 This Article shall only apply to the destruction of a document in good faith and without notice of any claim (regardless of the parties to it) to which the document might be relevant. Nothing in this Article shall be construed as imposing any liability on the Company in respect of the destruction of any such document other than as provided for in this Article which would not attach to the Company in the absence of this Article. References in this Article to the destruction of any document include references to the disposal of it in any manner.

42.4 References in this Article to instruments of transfer shall include, in relation to uncertificated shares, instructions and/or notifications made in accordance with the relevant system relating to the transfer of such shares.

43 **Sub-Division**

Any resolution authorising the Company to sub-divide its shares or any of them may determine that, as between the shares resulting from the sub-division, any of them may have any preference or advantage or be subject to any restriction as compared with the others.

44 **Fractions**

If any shares are consolidated or consolidated and then divided, the Board has power to deal with any fractions of shares which result. If the Board decides to sell any shares representing fractions, it can do so for the best price reasonably obtainable and distribute the net proceeds of sale among members in proportion to their fractional entitlements. The Board can arrange for any shares representing fractions to be entered in the Register as certificated shares if they consider that this makes it easier to sell them. The Board can sell those shares to anyone, including the Company if the legislation allows, and may authorise any person to transfer or deliver the shares to the buyer or in accordance with the buyer's instructions. The buyer shall not be bound to see to the application of the purchase money, nor shall the buyer's title to the share be affected by any irregularity or invalidity in the proceedings in reference to the sale.

45 **Annual General Meetings**

An annual general meeting shall be held once a year, at such time (consistent with the terms of the Companies Acts) and place as may be determined by the Board.

46 **Convening of General Meetings**

46.1 All meetings other than annual general meetings shall be called general meetings. The Board may, whenever it thinks fit, and shall on requisition in accordance with the Companies Acts, proceed to convene a general meeting.

46.2 Subject always to Article 55.3, the Board may make whatever arrangements it considers fit to allow those entitled to do so to attend and participate in any general meeting.

46.3 The Board shall determine in relation to each general meeting the means of attendance at and participation in the meeting, including whether the persons entitled to attend and participate in the meeting shall be enabled to do so:

(a) subject to Article 55.3) by means of electronic facility or facilities pursuant to Article 47 (and for the avoidance of doubt, the Board shall be under no obligation to offer or provide such facility or facilities, whatever the circumstances); and/or

(b) by simultaneous attendance and participation at a satellite meeting place or places pursuant to Article 49.7.

46.4 Unless otherwise specified in the notice of meeting or determined by the chair of the meeting, a general meeting is deemed to take place at the place where the chair of the meeting is at the time of the meeting.

46.5 Two or more persons who may not be in the same place as each other attend a general meeting if their circumstances are such that if they have (or were to have) rights to speak and vote at that meeting, they are (or would be) able to exercise them.

46.6 A person is able to participate in a meeting if that person's circumstances are such that if he or she has (or were to have) rights in relation to the meeting, he or she is (or would be) able to exercise them.

46.7 In determining whether persons are attending or participating in a meeting, other than at a physical place or places, it is immaterial where any of them are or how they are able to communicate with each other.

46.8 A person is able to exercise the right to speak at a general meeting when that person is in a position to communicate to all those attending the meeting, during the meeting, any information or opinions which that person has on the business of the meeting.

46.9 A person is able to exercise the right to vote at a general meeting when:

(a) that person is able to vote, during the meeting (or, in the case of a poll, within the time period specified by the chair of the meeting) on resolutions put to the vote at the meeting; and

(b) that person's vote can be taken into account in determining whether or not such resolutions are passed at the same time as the votes of all the other persons attending the meeting.

46.10 If, at any general meeting at which members are entitled to participate by means of electronic facility or facilities determined by the Board pursuant to Article 47, any document is required to be on display or to be available for inspection at the meeting (whether prior to or for the duration of the meeting or both), the Company shall ensure that it is available in electronic form to persons entitled to inspect it for at least the required period of time, and this will be deemed to satisfy any such requirement.

47 **SIMULTANEOUS ATTENDANCE AND PARTICIPATION BY ELECTRONIC FACILITIES**

Without prejudice to Article 46.7, the Board may resolve to enable persons entitled to attend and participate in a general meeting to do so partly (but not wholly) by simultaneous attendance and participation by means of electronic facility or facilities, and may determine the means, or all different means, of attendance and participation used in relation to the general meeting. The members present in person or by proxy by means of an electronic facility or facilities (as so determined by the Board) shall be counted in the quorum for, and be entitled to participate in, the general meeting in question. That meeting shall be duly constituted and its proceedings valid if the chair is satisfied that adequate facilities are available throughout the meeting to ensure that members attending the meeting by all means (including the means of an electronic facility or facilities) are able to:

(a) participate in the business for which the meeting has been convened;

(b) hear all persons who speak at the meeting; and

(c) be heard by all other persons attending and participating in the meeting.

48 **Notice of General Meetings**

A general meeting shall be called by at least such minimum notice as is required or permitted by the Companies Acts. The period of notice shall in either case be exclusive of the day on which it is served or deemed to be served and of the day on which the meeting is to be held and shall be given to all members other than those who are not entitled to receive such notices from the Company. The Company may give such notice by any means or combination of means permitted by the Companies Acts.

49 **Contents of Notice of Meetings**

49.1 Every notice calling a general meeting (including any satellite meeting place or places determined pursuant to Article 47) shall specify the place, date and time of the meeting, and there shall appear with reasonable prominence in every such notice a statement that a member entitled to attend and vote is entitled to a proxy or (if he has more than one share) proxies to exercise all or any of his rights to attend, speak and vote and that a proxy need not be a member of the Company. Such notice shall also include the address of the website on which the information required by the Act is published, state the procedures with which members must comply in order to be able to attend and vote at the meeting (including the date by which they must comply), provide details of any forms to be used for the appointment of a proxy and state that a member has the right to ask questions at the meeting in accordance with the Act.

49.2 The notice shall specify the general nature of the business to be transacted at the meeting and shall set out the text of all resolutions to be considered by the meeting and shall state in each case whether it is proposed as an ordinary resolution or as a special resolution.

49.3 In the case of an annual general meeting, the notice shall also specify the meeting as such.

49.4 If pursuant to Article 47 the Board determines that a general meeting shall be held partly by means of electronic facility or facilities, the notice shall:

(a) include a statement to that effect;

(b) specify the means, or all different means, of attendance and participation thereat, and any access, identification and security arrangements determined pursuant to Article 59; and

(c) state how it is proposed that persons attending or participating in the meeting electronically should communicate with each other during the meeting.

49.5 The notice shall specify such arrangements as have at that time been made for the purpose of Article 49.7 or Article 60.

49.6 For the purposes of determining which persons are entitled to attend or vote at a meeting and how many votes a person may cast, the Company may specify in the notice of meeting a time, not more than 48 hours before the time fixed for the meeting (not taking into account non-working days) by which a person must be entered in the Register in order to have the right to attend or vote at the meeting or appoint a proxy to do so.

49.7 Without prejudice to Article 47, the Board may resolve to enable persons entitled to attend and participate in a general meeting to do so by simultaneous attendance and participation at a satellite meeting place or places anywhere in the world. The members present in person or by proxy at satellite meeting places shall be counted in the quorum for, and entitled to participate in, the general meeting in question, and the meeting shall be duly constituted and its proceedings valid if the chair is satisfied that adequate facilities are available throughout the meeting to ensure that members attending at all the meeting places are able to:

(a) participate in the business for which the meeting has been convened;

(b) hear all persons who speak (whether by the use of microphones, loudspeakers, audio-visual communications equipment or otherwise) in the principal meeting place and any satellite meeting place; and

(c) be heard by all other persons so present in the same way,

and the meeting shall be deemed to take place at the place where the chairman of the meeting presides (the principal meeting place, with any other location where that meeting takes place being referred in these Articles as a satellite meeting). The chair shall be present at, and the meeting shall be deemed to take place at, the principal meeting place and the powers of the chair shall apply equally to each satellite meeting place, including his or her power to adjourn the meeting as referred to in Article 56.

50 **Omission to Give Notice and Non-Receipt of Notice**

The accidental omission to give notice of any meeting or to send an instrument of proxy (where this is intended to be sent out with the notice) to or the non-receipt of either by, any person entitled to receive the same shall not invalidate the proceedings of that meeting.

51 **Postponement of General Meeting**

If the Board considers that it is impracticable or unreasonable to hold a general meeting on the date or at the time or place stated in the notice calling the meeting, it may postpone or move the meeting (or do both). The Board shall take reasonable steps to ensure that notice of the date, time and place of the rearranged meeting is given to any member trying to attend the meeting at the original time and place. Notice of the date, time and place of the rearranged meeting shall, if practicable, also be placed in at least two national newspapers published in the United Kingdom. Notice of the business to be transacted at such rearranged meeting shall not be required. If a meeting is rearranged in this way, appointments of proxy are valid if they are received as required by these Articles not less than 48 hours before the time appointed for holding the rearranged meeting and for the purpose of calculating this period, the Board can decide in their absolute discretion, not to take account of any part of a day that is not a working day. The Board may also postpone or move the rearranged meeting (or do both) under this Article.

52 **Quorum at General Meeting**

No business shall be transacted at any general meeting unless a quorum is present. If a quorum is not present a chairman of the meeting can still be chosen and this will not be treated as part of the business of the meeting. Two members present in person or by proxy and entitled to attend and to vote on the business to be transacted shall be a quorum.

53 **Procedure if Quorum Not Present**

If a quorum is not present within 15 minutes (or such longer interval as the chairman in his absolute discretion thinks fit) from the time appointed for holding a general meeting, or if a quorum ceases to be present during a meeting, the meeting shall be dissolved if convened on the requisition of members. In any other case, the meeting shall stand adjourned to another day, (not being less than ten clear days after the date of the original meeting), and at such time and place or places, with such means of attendance and participation (including partly, but not wholly, by means of electronic facility or facilities), as the chairman (or, in default, the Board) may determine. If at such adjourned meeting a quorum is not present within 15 minutes from the time appointed for holding the meeting, one person entitled to vote on the business to be transacted, being a member or a proxy for a member or a duly authorised

representative of a corporation which is a member, shall be a quorum and any notice of an adjourned meeting shall state this.

54 **Chairman of General Meeting**

54.1 The chairman of the Board shall preside at every general meeting of the Company. If there is no such chairman or if at any meeting he shall not be present within five minutes after the time appointed for holding the meeting, or shall be unwilling to act as chairman, the deputy chairman (if any) of the Board shall, if present and willing to act, preside at such meeting. If more than one deputy chairman is present they shall agree amongst themselves who is to take the chair or, if they cannot agree, the deputy chairman who has been in office as a director the longest shall take the chair.

54.2 If no chairman or deputy chairman shall be so present and willing to act, the Directors present shall choose one of their number to act or, if there be only one Director present, he shall be chairman if willing to act. If there be no Director present and willing to act, the members present and entitled to vote shall choose one of their number to be chairman of the meeting. Nothing in these Articles shall restrict or exclude any of the powers or rights of a chairman of a meeting which are given by law.

55 **Entitlement to Attend and Speak**

55.1 A Director (and any other person invited by the chairman to do so) may attend and speak at any general meeting and at any separate meeting of the holders of any class of shares of the Company, whether or not he is a member.

55.2 All persons seeking to attend and participate in a general meeting by way of electronic facility or facilities shall be responsible for maintaining adequate facilities to enable them to do so. Subject only to the requirement for the chair to adjourn a general meeting in accordance with the provisions of Article 56.2, any inability of a person or persons to attend or participate in a general meeting by way of electronic facility or facilities shall not invalidate the proceedings of that meeting.

55.3 Nothing in these Articles authorises or allows a general meeting to be held exclusively on an electronic basis.

56 **Adjournments**

56.1 The chairman may, with the consent of a meeting at which a quorum is present, and shall, if so directed by the meeting, adjourn any meeting from time to time (or indefinitely) and from place to place (or, in the case of a meeting held at a principal meeting place and one or more satellite meeting places, such other places) and/or from such electronic facility or facilities for attendance and participation to such other electronic facility or facilities as the meeting shall determine. However, without prejudice to any other power which he may have under these Articles (including the power to adjourn a meeting conferred by Article 56.2) or at common law, the chairman may, without the need for the consent of the meeting and before or after it has started and irrespective of whether a quorum is present, interrupt or adjourn any meeting from time to time (or indefinitely) and from place to place (or places in the case of a meeting to which Article 49.7 applies) or from electronic facility to electronic facility, or for an indefinite period if he is of the opinion that it has become necessary to do so in order to secure the proper and orderly conduct of the meeting or to give all persons entitled to do so a reasonable opportunity of attending, speaking and voting at the meeting or to ensure that the business of the meeting is properly disposed of.

56.2 If it appears to the chair that the facilities at the principal meeting place or any satellite meeting place or an electronic facility or facilities or security at any general meeting have become inadequate for the purposes referred to in Articles 47 or 49.7, or are otherwise not sufficient to allow the meeting to be conducted substantially in accordance with the provisions

set out in the notice of meeting, then the chair shall, without the consent of the meeting, interrupt or adjourn the general meeting.

56.3 All business conducted at a meeting up to the time of any adjournment shall, subject to Article 56.4, be valid.

56.4 The chair may specify that only the business conducted at the meeting up to a point in time which is earlier than the time of the adjournment is valid, if in his or her opinion, to do so would be more appropriate.

57 **Notice of Adjournment**

Any adjournment pursuant to Article 56 may, subject to the Act, be for such time and with such means of attendance and participation (including at such place or places and/or by means of such electronic facility or facilities) as the chair (or, in default, the Board) may in his, her or its absolute discretion determine, notwithstanding that by reason of the adjournment some members may be unable to attend and participate in the adjourned meeting. Whenever a meeting is adjourned for 14 days or more or indefinitely, at least seven clear days' notice, specifying the day, the time and the place or places of the adjourned meeting and the means of attendance and participation (including by means of electronic facility or facilities if applicable) as the chair (or, in default, the Board) may in his or her absolute discretion determine, and the general nature of the business to be transacted, shall be given in the same manner as in the case of the original meeting. Save as aforesaid and subject to the Act, no member shall be entitled to any notice of an adjournment or of the business to be transacted at any adjourned meeting.

58 **Business of Adjourned Meeting**

No business shall be transacted at any adjourned meeting other than the business which might properly have been transacted at the meeting from which the adjournment took place.

59 **Accommodation of Members, Security Arrangements and Orderly Conduct at General Meetings**

59.1 The Board may, for the purpose of controlling the level of attendance or ensuring the safety of those attending at any place specified for the holding of a general meeting, ensuring the security of the meeting and ensuring the future orderly conduct of the meeting, from time to time make such arrangements as it shall in its absolute discretion consider to be appropriate and may from time to time vary any such arrangements or make new arrangements therefor. Any decision made under this Article 59.1 shall be final and the entitlement of any member or proxy to attend a general meeting at such place (or places, in the case of a meeting to which Article 49.7 applies) shall be subject to any such arrangements as may be for the time being approved by the Board.

59.2 The Board may direct that any person wishing to attend any general meeting held at a physical place should provide evidence of identity and submit to such searches or other security arrangements or restrictions (including restrictions in items of personal property to be taken into the meeting) as the Board shall consider appropriate in the circumstances.

59.3 If a general meeting is held partly by means of an electronic facility or facilities pursuant to Article 47, the Board and the chairman may make any arrangement and impose any requirement or restriction that is:

(a) necessary to ensure the identification of those taking part by means of such electronic facility or facilities and the security of the electronic communication; and

(b) in its or his or her view, proportionate to those objectives.

59.4 In this respect, the Board may authorise any voting application, system or facility for attendance and participation as it sees fit.

59.5 The Board shall be entitled in its absolute discretion to authorise one or more persons (including the Directors, the company secretary or the chairman) to refuse physical or electronic entry to, or eject (physically or electronically) from, any meeting any person who fails to provide such evidence of identity or to submit to such searches or to otherwise comply with such security arrangements or restrictions as are required pursuant to this Article, or who causes the meeting to become disorderly.

59.6 Subject to the Act (and without prejudice to any other powers vested in the chairman of a meeting) when conducting a general meeting, the chairman may make whatever arrangement and take such action or give such directions as he or she considers, in his or her absolute discretion, to be appropriate or conducive to promote the orderly conduct of the meeting, to promote the conduct of the business laid down in the notice of the meeting with reasonable despatch and to maintain good order. The chairman's decision on points of order, matters of procedure or on matters arising incidentally from the business of the meeting shall be final and conclusive, as shall his or her determination as to whether any point or matter is of such a natureSubject to the Act (and without prejudice to any other powers vested in the chairman of a meeting) when conducting a general meeting, the chairman may make whatever arrangement and take such action or give such directions as he or she considers, in his or her absolute discretion, to be appropriate or conducive to promote the orderly conduct of the meeting, to promote the conduct of the business laid down in the notice of the meeting with reasonable despatch and to maintain good order. The chairman's decision on points of order, matters of procedure or on matters arising incidentally from the business of the meeting shall be final and conclusive, as shall his or her determination as to whether any point or matter is of such a nature.

60 **Overflow Meeting Rooms**

60.1 The Board may, in accordance with this Article, make arrangements for members and proxies who are entitled to attend and participate in a general meeting, but who cannot be seated in the main meeting room where the chairman will be, to attend and take part in a general meeting in an overflow room or rooms. Any overflow room will have appropriate links to the main room and will enable audio-visual communication between the meeting rooms throughout the meeting. The Board will decide how to divide members and proxies between the main room and the overflow room. If an overflow room is used, the meeting will be treated as being held and taking place in the main meeting room and the meeting will consist of all the members and proxies who are attending both in the main meeting room and the overflow room.

60.2 Details of any arrangements for overflow rooms will be set out in the notice of the meeting but failure to do so will not invalidate the meeting.

61 **Amendment to Resolutions**

61.1 If an amendment to any resolution under consideration is proposed but is ruled out of order by the chairman of the meeting in good faith, any error in such ruling shall not invalidate the proceedings on the original resolution.

61.2 In the case of a resolution duly proposed as a special resolution, no amendment to it (other than an amendment to correct a patent error) may in any event be considered or voted on. In the case of a resolution duly proposed as an ordinary resolution no amendment to it (other than an amendment to correct a patent error) may be considered or voted on unless either at least 48 hours prior to the time appointed for holding the meeting or adjourned meeting at which such ordinary resolution is to be proposed, notice in writing of the terms of the amendment and intention to move the same has been lodged at the Office or received in electronic form at the electronic address at which the Company has or is deemed to have

agreed to receive it or the chairman of the meeting in his absolute discretion decides that it may be considered or voted on.

62 **Members' Resolutions**

62.1 Members of the Company shall have the rights provided by the Companies Acts to have the Company circulate and give notice of a resolution which may be properly moved, and is intended to be moved, at the Company's next annual general meeting.

62.2 Expenses of complying with these rights shall be borne in accordance with the Companies Acts.

63 **Method of Voting**

63.1 A resolution put to the vote at a general meeting held partly by means of electronic facility or facilities shall be decided on a poll, which poll votes may be cast by such electronic means as the Board, in its sole discretion, deems appropriate for the purposes of the meeting. Any such poll shall be deemed to have been validly demanded at the time fixed for the holding of the meeting to which it relates. Subject thereto, at any general meeting a resolution put to a vote of the meeting shall be decided on a show of hands, unless (before or on the declaration of the result of the show of hands) a poll is duly demanded. Subject to the Companies Acts, a poll may be demanded by:

(a) the chairman of the meeting; or

(b) at least two members present in person (or by proxy) and entitled to vote at the meeting; or

(c) a member or members present in person (or by proxy) representing at least one-tenth of the total voting rights of all the members having the right to vote at the meeting; or

(d) a member or members present in person (or by proxy) holding shares conferring a right to vote at the meeting, being shares on which an aggregate sum has been paid up equal to at least one-tenth of the total sum paid up on all the shares conferring that right.

63.2 The chairman of the meeting may also demand a poll before a resolution is put to the vote on a show of hands.

63.3 At general meetings, resolutions shall be put to the vote by the chairman of the meeting and there shall be no requirement for the resolution to be proposed or seconded by any person.

63.4 Unless a poll is duly demanded and the demand is not withdrawn, a declaration by the chairman of the meeting that a resolution has on a show of hands been carried, or carried unanimously or by a particular majority, or lost, or not carried by a particular majority, and an entry to that effect in the book containing the minutes of proceedings of the Company, shall be conclusive evidence of the fact, without proof of the number or proportion of the votes recorded in favour of or against such resolution.

64 **Objection to Error in Voting**

No objection shall be raised to the qualification of any voter or to the counting of, or failure to count, any vote, except at the meeting or adjourned meeting at which the vote objected to is given or tendered or at which the error occurs. Any objection or error shall be referred to the chairman of the meeting and shall only vitiate the decision of the meeting on any resolution if the chairman decides that the same is of sufficient magnitude to vitiate the resolution or may

otherwise have affected the decision of the meeting. The decision of the chairman of the meeting on such matters shall be final and conclusive.

65 **Procedure on a Poll**

65.1 Any poll duly demanded on the election of a chairman or on any question of adjournment shall be taken immediately. A poll duly demanded on any other matter shall be taken in such manner (including the use of ballot or voting papers or tickets or electronic means or any combination thereof) and at such time and place, not more than 30 days from the date of the meeting or adjourned meeting at which the poll was demanded, and by such means of attendance and participation (including at such place or places and/or by means of such electronic facility or facilities) as the chairman shall direct. The chairman may appoint scrutineers who need not be members. It is not necessary to give notice of a poll not taken immediately if the time and place at which it is to be taken are announced at the meeting at which it is demanded. In any other case, at least seven clear days' notice shall be given specifying the time, date and place at which the poll shall be taken. The result of the poll shall be deemed to be the resolution of the meeting at which the poll was demanded.

65.2 The demand for a poll (other than on the election of a chairman or any question of adjournment) shall not prevent the continuance of the meeting for the transaction of any business other than the question on which a poll has been demanded.

65.3 The demand for a poll may, before the poll is taken, be withdrawn, but only with the consent of the chairman of the meeting. A demand so withdrawn validates the result of a show of hands declared before the demand was made. If a poll is demanded before the declaration of the result of a show of hands and the demand is duly withdrawn, the meeting shall continue as if the demand had not been made.

65.4 On a poll votes may be given in person or by proxy. A member entitled to more than one vote need not, if he votes, use all his votes or cast all the votes he uses in the same way.

66 **Votes of Members**

66.1 Subject to Article 66.2, the Companies Acts, to any special terms as to voting on which any shares may have been issued or may for the time being be held and to any suspension or abrogation of voting rights under these Articles, at any general meeting every member who is present in person (or by proxy) shall on a show of hands have one vote and every member present in person (or by proxy) shall on a poll have one vote for each share of which he is the holder.

66.2 On a show of hands, a duly appointed proxy has one vote for and one vote against a resolution if the proxy has been appointed by more than one member entitled to vote on the resolution and the proxy has been instructed:

(a) by one or more of those members to vote for the resolution and by one or more other of those members to vote against it; or

(b) by one or more of those members to vote either for or against the resolution and by one or more other of those members to use his/her discretion as to how to vote.

66.3 If two or more persons are joint holders of a share, then in voting on any question the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other joint holders. For this purpose seniority shall be determined by the order in which the names of the holders stand in the Register.

66.4 Where in England or elsewhere a receiver or other person (by whatever name called) has been appointed by any court claiming jurisdiction in that behalf to exercise powers with respect to the property or affairs of any member on the ground (however formulated) of

mental disorder, the Board may in its absolute discretion, upon or subject to production of such evidence of the appointment as the Board may require, permit such receiver or other person on behalf of such member to vote in person, on a show of hands or on a poll, by proxy on behalf of such member at any general meeting or to exercise any other right conferred by membership in relation to meetings of the Company. Evidence to the satisfaction of the Board of the authority of the person claiming to exercise the right to vote shall be deposited at the Office, or at such other place as is specified in accordance with these Articles for the deposit of instruments of proxy, at least 48 hours before the time appointed for holding the meeting or adjourned meeting at which the right to vote is to be exercised and, in default, the right to vote shall not be exercisable.

66.5 In the case of equality of votes whether on a show of hands or on a poll, the chairman of the meeting at which the show of hands takes place or at which the poll is demanded shall not be entitled to a casting vote.

67 **No Right to Vote Where Sums Overdue on Shares**

No member may vote at a general meeting (or any separate meeting of the holders of any class of shares), either in person or by proxy, or to exercise any other right or privilege as a member in respect of a share held by him unless:

(a) all calls or other sums presently due and payable by him in respect of that share whether alone or jointly with any other person together with interest and expenses (if any) have been paid to the Company; or

(b) the Board determines otherwise.

68 **Voting by Proxy**

68.1 Subject to Article 68.2, an instrument appointing a proxy shall be in writing in any usual form (or in another form approved by the Board) executed under the hand of the appointer or his duly constituted attorney or, if the appointer is a corporation, under its seal or signed by a duly authorised officer or attorney or other person authorised to sign.

68.2 Subject to the Companies Acts, the Board may accept the appointment of a proxy received by electronic means on such terms and subject to such conditions as it considers fit. The appointment of a proxy received by electronic means shall not be subject to the requirements of Article 68.1.

68.3 For the purposes of Articles 68.1 and 68.2, the Board may require such reasonable evidence it considers necessary to determine:

(a) the identity of the member and the proxy; and

(b) where the proxy is appointed by a person acting on behalf of the member, the authority of that person to make the appointment.

68.4 A member may appoint another person as his proxy to exercise all or any of his rights to attend and to speak and to vote (both on a show of hands and on a poll) on a resolution or amendment of a resolution, or on other business arising, at a meeting or meetings of the Company. Unless the contrary is stated in it, the appointment of a proxy shall be deemed to confer authority to exercise all such rights, as the proxy thinks fit.

68.5 A proxy need not be a member.

68.6 A member may appoint more than one proxy in relation to a meeting, provided that each proxy is appointed to exercise the rights attached to different shares held by the member. When two or more valid but differing appointments of proxy are delivered or received for the

same share for use at the same meeting, the one which is last validly delivered or received (regardless of its date or the date of its execution) shall be treated as replacing and revoking the other or others as regards that share. If the Company is unable to determine which appointment was last validly delivered or received, none of them shall be treated as valid in respect of that share.

68.7 Delivery or receipt of an appointment of proxy does not prevent a member attending and voting in person at the meeting or an adjournment of the meeting or on a poll.

68.8 The appointment of a proxy shall (unless the contrary is stated in it) be valid for an adjournment of the meeting as well as for the meeting or meetings to which it relates. The appointment of a proxy shall be valid for 12 months from the date of execution or, in the case of an appointment of proxy delivered by electronic means, for 12 months from the date of delivery unless otherwise specified by the Board.

68.9 Subject to the Companies Acts, the Company may send a form of appointment of proxy to all or none of the persons entitled to receive notice of and to vote at a meeting. If sent, the form shall provide for three-way voting on all resolutions (other than procedural resolutions) set out in the notice of meeting.

69 **Receipt of Proxy**

69.1 An instrument appointing a proxy and any reasonable evidence required by the Board in accordance with Article 68.3 shall:

(a) subject to Articles 69.1(c) and (d), in the case of an instrument of proxy in hard copy form, delivered to the office, or another place in the United Kingdom specified in the notice convening the meeting or in the form of appointment of proxy or other accompanying document sent by the Company in relation to the meeting (a **proxy notification address**) not less than 48 hours before the time for holding the meeting or adjourned meeting at which the person named in the form of appointment of proxy proposes to vote;

(b) subject to Articles 69.1(c) and (d), in the case of an appointment of a proxy sent by electronic means, where the Company has given an electronic address (a proxy notification electronic address):

(i) in the notice calling the meeting;

(ii) in an instrument of proxy sent out by the Company in relation to the meeting;

(iii) in an invitation to appoint a proxy issued by the Company in relation to the meeting; or

(iv) on a website maintained by or on behalf of the Company on which any information relating to the meeting is required by the Act to be kept,

it shall be received at such proxy notification electronic address not less than 48 hours before the time for holding the meeting or adjourned meeting at which the person named in the form of appointment of proxy proposes to vote;

(c) in the case of a poll taken more than 48 hours after it is demanded, delivered or received at a proxy notification address or a proxy notification electronic address and not less than 24 hours before the time appointed for the holding of the adjourned meeting or the taking of the poll; or

(d) in the case of a poll which is not taken at the meeting at which it is demanded but is taken 48 hours or less after it is demanded, or in the case of an adjourned meeting to be held 48 hours or less after the time fixed for holding the original meeting, received:

(i) at a proxy notification address or a proxy notification electronic address in accordance with Articles 69.1(a) or (b);

(ii) by the chairman of the meeting or the secretary or any director at the meeting at which the poll is demanded or, as the case may be, at the original meeting; or

(iii) at a proxy notification address or a proxy notification electronic address by such time as the chairman of the meeting may direct at the meeting at which the poll is demanded.

In calculating the periods in this Article, no account shall be taken of any part of a day that is not a working day.

69.2 The Board may decide, either generally or in any particular case, to treat a proxy appointment as valid notwithstanding that the appointment or any of the information required under Article 68.3 has not been received in accordance with the requirements of this Article.

69.3 Subject to Article 69.2, if the proxy appointment and any of the information required under Article 68.3 is not received in the manner set out in Article 69.1, the appointee shall not be entitled to vote in respect of the shares in question.

69.4 Without limiting the foregoing, in relation to any uncertificated shares, the Board may from time to time:

(a) permit appointments of a proxy by means of a communication sent in electronic form in the form of an uncertificated proxy instruction; and

(b) permit supplements to, or amendments or revocations of, any such uncertificated proxy instruction by the same means.

The Board may in addition prescribe the method of determining the time at which any such uncertificated proxy instruction is to be treated as received by the Company or a participant acting on its behalf. The Board may treat any such uncertificated proxy instruction which purports to be or is expressed to be sent on behalf of a holder of a share as sufficient evidence of the authority of the person sending that instruction to send it on behalf of that holder.

70 **Revocation of Proxy**

A vote given or poll demanded by a proxy shall be valid in the event of the death or mental disorder of the principal or the revocation of the instrument of proxy, or of the authority under which the instrument of proxy was executed, or the transfer of the share for which the instrument of proxy is given, unless notice in writing of such death, mental disorder, revocation or transfer shall have been received by the Company at the Office, or at such other place as has been appointed for the deposit of instruments of proxy, no later than the last time at which an appointment of a proxy should have been received in order for it to be valid for use at the meeting or on the holding of the poll at which the vote was given or the poll taken.

71 **Corporate Representatives**

71.1 A corporation (whether or not a company within the meaning of the Act) which is a member may, by resolution of its directors or other governing body, authorise such person as it thinks fit to act as its representative (or, as the case may be, representatives) at any meeting of the Company or at any separate meeting of the holders of any class of shares.

71.2 Any person so authorised shall be entitled to exercise the same powers on behalf of the corporation (in respect of that part of the corporation's holdings to which the authority relates) as the corporation could exercise if it were an individual member.

71.3 The corporation shall for the purposes of these Articles be deemed to be present in person and at any such meeting if a person so authorised is present at it, and all references to attendance and voting in person shall be construed accordingly.

71.4 A Director, the Secretary or some person authorised for the purpose by the Secretary may require the representative to produce a certified copy of the resolution so authorising him or such other evidence of his authority reasonably satisfactory to them before permitting him to exercise his powers.

71.5 A vote given or a poll demanded by a corporate representative shall be valid notwithstanding that the representative is no longer authorised to represent the member unless notice of the revocation of appointment was delivered in writing to the Company at such place or address and by such time as is specified in Article 70 for the revocation of the appointment of a proxy.

72 **Failure to Disclose Interests in Shares**

72.1 If a member, or any other person appearing to be interested in shares held by that member, has been issued with a notice under section 793 of the Act (**section 793 notice**) and has failed in relation to any shares (**default shares,** which expression includes any shares issued after the date of such notice in right of those shares) to give the Company the information required by the section 793 notice within the prescribed period from the service of the notice, the following sanctions shall apply unless the Board determines otherwise:

(a) the member shall not be entitled in respect of the default shares to be present or to vote (either in person or by representative or proxy) at any general meeting or at any separate meeting of the holders of any class of shares or on any poll or to exercise any other right conferred by membership in relation to any such meeting or poll; and

(b) where the default shares represent at least 0.25% in nominal value of the issued shares of their class (calculated exclusive of any shares held as treasury shares):

(i) any dividend or other money payable for such shares shall be withheld by the Company, which shall not have any obligation to pay interest on it, and the member shall not be entitled to elect, pursuant to Article 130, to receive shares instead of that dividend; and

(ii) no transfer, other than an excepted transfer, of any shares held by the member shall be registered unless the member himself is not in default of supplying the required information and the member proves to the satisfaction of the Board that no person in default of supplying such information is interested in any of the shares that are the subject of the transfer.

For the purposes of ensuring Article 72.1(b)(ii) can apply to all shares held by the member, the Company may in accordance with the uncertificated securities rules, issue a written notification to the Operator requiring conversion into certificated form of any share held by the member in uncertificated form.

72.2 Where the sanctions under Article 72.1 apply in relation to any shares, they shall cease to have effect (and any dividends withheld under Article 72.1(b) shall become payable):

(a) if the shares are transferred by means of an excepted transfer but only in respect of the shares transferred; or

(b) at the end of the period of seven days (or such shorter period as the Board may determine) following receipt by the Company of the information required by the section 793 notice and the Board being fully satisfied that such information is full and complete.

72.3 Where, on the basis of information obtained from a member in respect of any share held by him, the Company issues a section 793 notice to any other person, it shall at the same time send a copy of the notice to the member, but the accidental omission to do so, or the non-receipt by the member of the copy, shall not invalidate or otherwise affect the application of Article 72.1.

72.4 For the purposes of this Article:

(a) a person, other than the member holding a share, shall be treated as appearing to be interested in that share if the member has informed the Company that the person is, or may be, so interested, or if the Company (after taking account of any information obtained from the member or, pursuant to a section 793 notice, from anyone else) knows or has reasonable cause to believe that the person is, or may be, so interested;

(b) **interested** shall be construed as it is for the purpose of section 793 of the Act;

(c) reference to a person having failed to give the Company the information required by a notice, or being in default as regards supplying such information, includes reference:

(i) to his having failed or refused to give all of any part of it; and

(ii) to his having given information which he knows to be false in a material particular or having recklessly given information which is false in a material particular;

(d) **prescribed period** means 14 days;

(e) **excepted transfer** means, in relation to any shares held by a member:

(i) a transfer by way of or pursuant to acceptance of a takeover offer for the Company (within the meaning of section 974 of the Act); or

(ii) a transfer in consequence of a sale made through a recognised investment exchange (as defined in section 285 of the FSMA) or any other stock exchange outside the United Kingdom on which the Company's shares are normally traded; or

(iii) a transfer which is shown to the satisfaction of the Board to be made in consequence of a sale of the whole of the beneficial interest in the

shares to a person who is unconnected with the member and with any other person appearing to be interested in the shares.

72.5 Nothing contained in this Article shall be taken to limit the powers of the Company under section 794 of the Act.

73 **Power of Sale of Shares of Untraced Members**

73.1 The Company shall be entitled to sell at the best price reasonably obtainable any share of a member, or any share to which a person is entitled by transmission, if and provided that:

(a) during the period of 12 years before the date of sending of the notice referred to in Article 73.1(b) no cheque, order or warrant in respect of such share sent by the Company through the post in a pre-paid envelope addressed to the member or to the person entitled by transmission to the share, at his address on the Register or other last known address given by the member or person to which cheques, orders or warrants in respect of such share are to be sent has been cashed and the Company has received no communications in respect of such share from such member or person entitled, provided that during such period of 12 years the Company has paid at least three cash dividends (whether interim or final) and no such dividend has been claimed by the person entitled to it;

(b) on or after expiry of the said period of 12 years, the Company has given notice of its intention to sell such share by sending a notice to the member or person entitled by transmission to the share at his address on the Register or other last known address given by the member or person entitled by transmission to the share and before sending such a notice to the member or other person entitled by transmission, the Company must have used reasonable efforts to trace the member or other person entitled, engaging, if considered appropriate, a professional asset reunification company or other tracing agent and/or giving notice of its intention to sell the share by advertisement in a national newspaper and in a newspaper circulating in the area of the address of the member or person entitled by transmission to the share shown in the Register;

(c) during the further period of three months following the date of such notice and prior to the exercise of the power of sale the Company has not received any communication in respect of such share from the member or person entitled by transmission; and

(d) the Company has given notice to NASDAQ of its intention to make such sale, if shares of the class concerned, or certificated or uncertificated depositary instruments over such shares, are listed on NASDAQ or dealt in on any other recognised stock exchange on which the shares are listed.

73.2 To give effect to any sale of shares under this Article, the Board may authorise some person to transfer the shares in question and may enter the name of the transferee in respect of the transferred shares in the Register even if no share certificate has been lodged for such shares and may issue a new certificate to the transferee. An instrument of transfer executed by that person shall be as effective as if it had been executed by the holder of or the person entitled by transmission to, the shares. The buyer shall not be bound to see to the application of the purchase monies, nor shall his title to the shares be affected by any irregularity or invalidity in the proceedings in reference to the sale. If the shares are in uncertificated form, in accordance with the uncertificated securities rules, the Board may issue a written notification to the Operator requiring the conversion of the share to certificated form.

73.3 If during the period of 12 years referred to in Article 73.1, or during any period ending on the date when all the requirements of Articles 73.1(a) to 73.1(d) have been satisfied, any additional shares have been issued in respect of those held at the beginning of, or previously so issued during, any such period and all the requirements of Articles 73.1(b) to 73.1(d) have been satisfied in regard to such additional shares, the Company shall also be entitled to sell the additional shares.

74 **Application of Proceeds of Sale of Shares of Untraced Members**

The Company shall account to the member or other person entitled to the share for the net proceeds of a sale under Article 73 by carrying all monies relating to such sale to a separate account. The Company shall be deemed to be a debtor to, and not a trustee for, such member or other person in respect of such monies. Monies carried to such separate account may either be employed in the business of the Company or invested in such investments as the Board may think fit. No interest shall be payable to such member or other person in respect of such monies and the Company does not have to account for any money earned on them.

75 **Number of Directors**

Unless otherwise determined by the Company by ordinary resolution, the number of Directors (other than any alternate Directors) shall be at least two.

76 **Power of Company to Appoint Directors**

Subject to these Articles and the Companies Acts, the Company may by ordinary resolution appoint a person who is willing to act to be a Director, either to fill a vacancy or as an addition to the existing Board but the total number of Directors shall not exceed any maximum number fixed in accordance with these Articles.

77 **Power of Board to Appoint Directors**

Subject to these Articles, the Board shall have power at any time to appoint any person who is willing to act as a Director, either to fill a vacancy or as an addition to the existing Board but the total number of Directors shall not exceed any maximum number fixed in accordance with these Articles.

78 **Eligibility of New Directors**

78.1 No person, other than a retiring Director (by rotation or otherwise), shall be appointed or re-appointed a Director at any general meeting unless:

(a) he is recommended by the Board; or

(b) at least seven but not more than 42 clear days before the date appointed for the meeting the Company has received notice from a member (other than the person proposed) entitled to vote at the meeting of his intention to propose a resolution for the appointment or re-appointment of that person, stating the particulars which would, if he were so appointed or re-appointed, be required to be included in the Company's register of directors and a notice executed by that person of his willingness to be appointed or re-appointed, is lodged at the Office.

78.2 A Director need not be a member of the Company.

79 **Retirement of Directors**

79.1 The Directors shall be divided into three classes designated as "Class I", "Class II", and "Class III", respectively. The Board is authorised to assign members of the Board already in office such classes at the time the Listing becomes effective.

79.2 At the first annual general meeting of the Company following the Listing, each Director in Class I shall retire from office but shall be eligible for re-appointment by ordinary resolution at such annual general meeting and, in each case, where such Director is so re-appointed, they shall be entitled to serve until the third anniversary of such annual general meeting of the Company, at which stage such Director shall retire from office but shall be eligible for reappointment.

79.3 At the second annual general meeting of the Company following the Listing, each Director in Class II shall retire from office but shall be eligible for re-appointment by ordinary resolution at such annual general meeting and, in each case, where such Director is so re-appointed, they shall be entitled to serve until the third anniversary of such annual general meeting of the Company, at which stage such Director shall retire from office but shall be eligible for reappointment.

79.4 At the third annual general meeting of the Company following the Listing, each Director in Class III shall retire from office but shall be eligible for re-appointment by ordinary resolution at such annual general meeting and, in each case, where such Director is so re-appointed, they shall be entitled to serve until the third anniversary of such annual general meeting of the Company, at which stage such Director shall retire from office but shall be eligible for reappointment.

79.5 At each succeeding annual general meeting of the Company following the third annual general meeting of the Company after the Listing. Directors shall be elected to serve for a term of three years to succeed the Directors of the class whose terms expire at such annual general meeting.

79.6 Notwithstanding the foregoing provisions, each Director shall serve until their successor is duly elected and qualified or until their earlier death resignation or removal.

80 **Deemed Re-Appointment**

80.1 A Director who retires at an annual general meeting shall (unless he is removed from office or his office is vacated in accordance with these Articles) retain office until the close of the meeting at which he retires or (if earlier) when a resolution is passed at that meeting not to fill the vacancy or to elect another person in his place or the resolution to re-appoint him is put to the meeting and lost.

80.2 If the Company, at any meeting at which a Director retires in accordance with these Articles does not fill the office vacated by such Director, the retiring Director, if willing to act, shall be deemed to be re-appointed unless at that meeting a resolution is passed not to fill the vacancy or elect another person in his place or unless the resolution to re-appoint him is put to the meeting and lost.

81 **Procedure if Insufficient Directors Appointed**

81.1 If:

(a) at the annual general meeting in any year any resolution or resolutions for the appointment or re-appointment of the persons eligible for appointment or re-appointment as Directors are put to the meeting and lost; and

(b) at the end of that meeting the number of Directors is fewer than any minimum number of Directors required under Article 75,

all retiring Directors who stood for re-appointment at that meeting (**Retiring Directors**) shall be deemed to have been re-appointed as Directors and shall remain in office but the Retiring Directors may only act for the purpose of filling vacancies, convening general meetings of the Company and performing such duties as are essential to maintain the Company as a going concern, and not for any other purpose.

81.2 The Retiring Directors shall convene a general meeting as soon as reasonably practicable following the meeting referred to in Article 81.1 and they shall retire from office at that meeting. If at the end of any meeting convened under this Article the number of Directors is fewer than any minimum number of Directors required under Article 75, the provisions of this Article shall also apply to that meeting.

82 **Removal of Directors**

In addition to any power of removal conferred by the Companies Acts, the Company may by special resolution, or by ordinary resolution of which special notice has been given in accordance with section 312 of the Act, remove a director before the expiry of his period of office (without prejudice to a claim for damages for breach of contract or otherwise) and may (subject to these Articles) by ordinary resolution appoint another person who is willing to act to be a director in his place.

83 **Vacation of Office by Director**

83.1 Without prejudice to the provisions for retirement (by rotation or otherwise) contained in these Articles, the office of a Director shall be vacated if:

(a) he resigns by notice in writing delivered to the Secretary at the Office or at an address specified by the Company for the purposes of communication by electronic means or tendered at a Board meeting;

(b) he offers to resign by notice in writing delivered to the Secretary at the Office or at an address specified by the Company for the purposes of communication by electronic means or tendered at a Board meeting and the Board resolves to accept such offer;

(c) he is requested to resign by all of the other Directors by notice in writing addressed to him at his address as shown in the register of Directors (without prejudice to any claim for damages which he may have for breach of any contract between him and the Company);

(d) he ceases to be a Director by virtue of any provision of the Companies Acts, is removed from office pursuant to these Articles or the Act or becomes prohibited by law from being a Director;

(e) he becomes bankrupt or makes an arrangement or composition with his creditors generally;

(f) a registered medical practitioner who is treating that person gives a written opinion to the Company stating that person has become physically or mentally incapable of acting as a director and may remain so for more than three months, or he is or has been suffering from mental or physical ill health and the Board resolves that his office be vacated; or

(g) he is absent (whether or not his alternate Director appointed by him attends), without the permission of the Board, from Board meetings for six consecutive months and a notice is served on him personally, or at his residential address provided to the Company under section 165 of the Act signed by all the other Directors stating that he shall cease to be a Director with immediate effect (and such notice may consist of several copies each signed by one or more Directors).

83.2 If the office of a Director is vacated for any reason, he shall cease to be a member of any committee or sub-committee of the Board.

84 **Resolution as to Vacancy Conclusive**

A resolution of the Board declaring a Director to have vacated office under the terms of Article 83 shall be conclusive as to the fact and ground of vacation stated in the resolution.

85 **Appointment of Alternate Directors**

85.1 Each Director may appoint any person (including another Director) to be his alternate and may at his discretion remove an alternate Director so appointed. Any appointment or removal of an alternate Director must be by written notice delivered to the Office or at an address specified by the Company for the purposes of communication by electronic means or tendered at a Board meeting or in any other manner approved by the Board. The appointment requires the approval of the Board unless it has been previously approved or the appointee is another Director.

85.2 An alternate Director must provide the particulars, and sign any form for public filing required by the Companies Acts relating to his appointment.

86 **Alternate Directors' Participation in Board Meetings**

86.1 Every alternate Director is (subject to his giving to the Company an address within the United Kingdom at which notices may be served on him (and, if applicable, an address in relation to which electronic communications may be received by him)) entitled to receive notice of all meetings of the Board and all committees of the Board of which his appointor is a member and, in his appointor's absence, to attend and vote at such meetings and to exercise all the powers, rights, duties and authorities of his appointor. Each person acting as an alternate Director shall have a separate vote at Board meetings for each Director for whom he acts as alternate Director in addition to his own vote if he is also a Director, but he shall count as only one for the purpose of determining whether a quorum is present.

86.2 Signature by an alternate Director of any resolution in writing of the Board or a committee of the Board will, unless the notice of his appointment provides otherwise, be as effective as signature by his appointor.

87 **Alternate Directors Responsible for Own Acts**

Each person acting as an alternate Director will be an officer of the Company, will alone be responsible to the Company for his own acts and defaults and will not be deemed to be the agent of the Director appointing him.

88 **Interests of Alternate Director**

An alternate Director is entitled to contract and be interested in and benefit from contracts or arrangements with the Company, to be repaid expenses and to be indemnified to the same extent as if he were a Director. However, no alternative Director is entitled to receive from the Company any fees for his services as alternate, except such part (if any) of the fee payable to the alternative's appointor as such appointor may by written notice to the Company direct.

89 **Revocation of Alternate Director**

An alternate Director will cease to be an alternate Director:

(a) if his appointor revokes his appointment; or

(b) if he resigns his office by notice in writing to the Company; or

(c) if his appointor ceases for any reason to be a Director, provided that if any Director retires but is re-appointed or deemed to be re-appointed at the same meeting, any valid appointment of an alternate Director which was in force immediately before his retirement shall remain in force; or

(d) if any event happens in relation to him which, if he were a Director otherwise appointed, would cause him to vacate his office.

90 **Directors' Fees**

Each of the Directors may be paid a fee at such rate as may from time to time be determined by the Board. However, the aggregate of all fees payable to the Directors (other than amounts payable under any other provision of these Articles) must not exceed £1,000,000 a year or such higher amount as may from time to time be decided by ordinary resolution of the Company. Any fees payable under this Article shall be distinct from any salary, remuneration or other amounts payable to a Director under any other provisions of these Articles and shall accrue from day to day.

91 **Expenses**

Each Director may be paid his reasonable travelling, hotel and other expenses properly incurred by him in or about the performance of his duties as Director, including any expenses incurred in attending meetings of the Board or any committee of the Board or general meetings or separate meetings of the holders of any class of shares or debentures of the Company. Subject to the Act, the Directors shall have the power to make arrangements to provide a Director with funds to meet expenditure incurred or to be incurred by him for the purposes of the Company or for the purpose of enabling him to perform his duties as an officer of the Company or to enable him to avoid incurring any such expenditure.

92 **Additional Remuneration**

If by arrangement with the Board any Director shall perform or render any special duties or services outside his ordinary duties as a Director and not in his capacity as a holder of employment or executive office, he may be paid such reasonable additional remuneration (whether by way of salary, commission, participation in profits or otherwise) as the Board may determine.

93 **Remuneration of Executive Directors**

The salary or remuneration of any Director appointed to hold any employment or executive office in accordance with these Articles may be either a fixed sum of money, or may altogether or in part be governed by business done or profits made or otherwise determined by the Board, and may be in addition to or instead of any fee payable to him for his services as Director under these Articles.

94 **Pensions and Other Benefits**

94.1 The Board may exercise all the powers of the Company to provide pensions or other retirement or superannuation benefits and to provide death or disability benefits or other

allowances or gratuities (whether by insurance or otherwise) for any person who is or has at any time been a Director or employee of:

(a) the Company;

(b) any company which is or was a holding company or a subsidiary undertaking of the Company;

(c) any company which is or was allied to or associated with the Company or a subsidiary undertaking or holding company of the Company; or

(d) a predecessor in business of the Company or of any holding company or subsidiary undertaking of the Company,

and, in each case, for any member of his family (including a spouse or former spouse) and any person who is or was dependent on him.

94.2 The Board may establish, maintain, subscribe and contribute to any scheme, institution, association, club, trust or fund and pay premiums and, subject to the Companies Acts, lend money or make payments to, guarantee or give an indemnity in respect of, or give any financial or other assistance in connection with any of the matters set out in Article 94.1 above. The Board may procure any of such matters to be done by the Company either alone or in conjunction with any other person. Any Director or former Director shall be entitled to receive and retain for his own benefit any pension or other benefit provided under this Article and shall not have to account for it to the Company. The receipt of any such benefit will not disqualify any person from being or becoming a Director of the Company.

95 **Powers of the Board**

95.1 Subject to the Companies Acts, these Articles and to any directions given by special resolution of the Company, the business of the Company will be managed by the Board, which may exercise all the powers of the Company, whether relating to the management of the business or not.

95.2 No alteration of these Articles and no such direction given by the Company shall invalidate any prior act of the Board which would have been valid if such alteration had not been made or such direction had not been given. Provisions contained elsewhere in these Articles as to any specific power of the Board shall not be deemed to limit the general powers given by this Article.

96 **Powers of Directors if Less Than Minimum Number**

If the number of Directors is less than the minimum prescribed in Article 75 or decided by the Company by ordinary resolution, the remaining Director or Directors may act only for the purposes of appointing an additional Director or Directors to make up that minimum or convening a general meeting of the Company for the purpose of making such appointment. If no Director or Directors is or are able or willing to act, two members may convene a general meeting for the purpose of appointing Directors. An additional Director appointed in this way holds office (subject to these Articles) only until the dissolution of the next annual general meeting after his appointment unless he is reappointed during the annual general meeting.

97 **Powers of Executive Directors**

The Board or any committee authorised by the Board may:

(a) delegate or entrust to and confer on any Director holding executive office (including a chief executive or managing director, if appointed) such of its powers, authorities

and discretions (with power to sub-delegate) for such time, on such terms and subject to such conditions as it thinks fit; and

(b) revoke, withdraw, alter or vary all or any of such powers.

98 **Delegation to Committees**

98.1 The Board may delegate any of its powers, authorities and discretions (with power to sub-delegate) for such time on such terms and subject to such conditions as it thinks fit to any committee consisting of one or more Directors and (if thought fit) one or more other persons provided that:

(a) a majority of the members of a committee shall be Directors; and

(b) no resolution of a committee shall be effective unless a majority of those present when it is passed are Directors or alternate Directors.

98.2 The Board may confer such powers either collaterally with, or to the exclusion of and in substitution for, all or any of the powers of the Board in that respect and may revoke, withdraw, alter or vary any such powers and discharge any such committee in whole or in part. Insofar as any power, authority or discretion is so delegated, any reference in these Articles to the exercise by the Board of such power, authority or discretion shall be construed as if it were a reference to the exercise of such power, authority or discretion by such committee.

99 **Local Management**

99.1 The Board may establish any local or divisional boards or agencies for managing any of the affairs of the Company in any specified locality, either in the United Kingdom or elsewhere, and appoint any persons to be members of such local or divisional board, or any managers or agents, and may fix their remuneration.

99.2 The Board may delegate to any local or divisional board, manager or agent so appointed any of its powers, authorities and discretions (with power to sub-delegate) and may authorise the members of any such local or divisional board, or any of them, to fill any vacancies and to act notwithstanding vacancies. Any such appointment or delegation under this Article may be made, on such terms conditions as the Board may think fit. The Board may confer such powers either collaterally with, or to the exclusion of and in substitution for, all or any of the powers of the Board in that respect and may revoke, withdraw, alter or vary all or any of such powers.

99.3 Subject to any terms and conditions expressly imposed by the Board, the proceedings of any local or divisional board or agency with two or more members shall be governed by such of these Articles as regulate the proceedings of the Board, so far as they are capable of applying.

100 **Board Meetings**

100.1 The Board can decide when and where to have meetings and how they will be conducted. They may also adjourn meetings.

100.2 A Board meeting can be called by any Director. The Secretary must call a Board meeting if asked to do so by a Director.

101 **Notice of Board Meetings**

101.1 Notice of a Board meeting shall be deemed to be duly given to a Director if it is given to him personally or by word of mouth or given in writing or by electronic means to him at his last known address or any other address given by him to the Company for that purpose.

101.2 A Director may waive the requirement that notice be given to him of any Board meeting, either prospectively or retrospectively and any retrospective waiver shall not affect the validity of the meeting or of any business conducted at the meeting.

101.3 It shall not be necessary to give notice of a Board meeting to a Director who is absent from the United Kingdom unless he has asked the Board in writing that notices of Board meetings shall during his absence be given to him at any address in the United Kingdom notified to the Company for this purpose, but he shall not, in such event, be entitled to a longer period of notice than if he had been present in the United Kingdom at that address.

102 **Quorum**

102.1 The quorum necessary for the transaction of business may be determined by the Board (but shall be no less than two persons) and until otherwise determined shall be two persons, each being a Director or an alternate Director. A duly convened meeting of the Board at which a quorum is present shall be competent to exercise all or any of the authorities, powers, and discretions for the time being vested in or exercisable by the Board.

102.2 If a Director ceases to be a director at a Board meeting, he can continue to be present and to act as a director and be counted in the quorum until the end of the meeting if no other Director objects and if otherwise a quorum of Directors would not be present.

103 **Chairman**

103.1 The Board may appoint one or more of its body as chairman or joint chairman and one or more of its body as deputy chairman of its meetings and may determine the period for which he is or they are to hold office and may at any time remove him or them from office.

103.2 If no such chairman or deputy chairman is elected, or if at any meeting neither a chairman nor a deputy chairman is present within ten minutes of the time appointed for holding the same, the Directors present shall choose one of their number to be chairman of such meeting. In the event two or more joint chairmen or, in the absence of a chairman, two or more deputy chairman being present, the joint chairman or deputy chairman to act as chairman of the meeting shall be decided by those Directors present.

104 **Voting**

Questions arising at any Board meeting shall be determined by a majority of votes. In the case of an equality of votes the chairman of that meeting shall have a second or casting vote (unless he is not entitled to vote on the resolution in question).

105 **Participation by Telephone or Other Form of Communication**

105.1 Any Director or his alternate may validly participate in a meeting of the Board or a committee of the Board through the medium of conference telephone or any other form of communications equipment (whether in use when these Articles are adopted or developed subsequently), provided that all persons participating in the meeting are able to hear and speak to each other throughout such meeting.

105.2 A person so participating by telephone or other communication shall be deemed to be present in person at the meeting and shall be counted in a quorum and entitled to vote. Such a meeting shall be deemed to take place where the largest group of those participating is

assembled or, if there is no group which is larger than any other group, where the chairman of the meeting then is.

105.3 A resolution passed at any meeting held in the above manner, and signed by the chairman of the meeting, shall be as valid and effectual as if it had been passed at a meeting of the Board (or committee, as the case may be) duly convened and held.

106 **Resolution in Writing**

106.1 A resolution in writing signed or confirmed electronically by all the Directors for the time being entitled to receive notice of a Board meeting and to vote on the resolution and not being less than a quorum (or by all the members of a committee of the Board for the time being entitled to receive notice of such committee meeting and to vote on the resolution and not being less than a quorum of that committee), shall be as valid and effective for all purposes as a resolution duly passed at a meeting of the Board (or committee, as the case may be).

106.2 Such a resolution may consist of several documents or electronic communications in the same form each signed or authenticated by one or more of the Directors or members of the relevant committee.

107 **Proceedings of Committees**

All committees of the Board shall, in the exercise of the powers delegated to them and in the transaction of business, conform with any mode of proceedings and regulations which the Board may prescribe and subject to this shall be governed by such of these Articles as regulate the proceedings of the Board as are capable of applying.

108 **Minutes of Proceedings**

108.1 The Board shall keep minutes of all shareholder meetings, all Board meetings and meetings of committees of the Board. The minutes must include the names of the Directors present.

108.2 Any such minutes, if purporting to be signed by the chairman of the meeting at which the proceedings were held or by the chairman of the next meeting or the Secretary, shall be evidence of the matters stated in such minutes without any further proof.

109 **Validity of Proceedings**

All acts done by a meeting of the Board, or of a committee of the Board, or by any person acting as a Director, alternate Director or member of a committee shall be valid even if it is discovered afterwards that there was some defect in the appointment of any person or persons acting, or that they or any of them were or was disqualified from holding office or not entitled to vote, or had in any way vacated their or his office.

110 **Transactions or Other Arrangements With the Company**

110.1 Subject to the Companies Acts and provided he has declared the nature and extent of his interest in accordance with the requirements of the Companies Acts, a Director who is in any way, whether directly or indirectly, interested in an existing or proposed transaction or arrangement with the Company may:

(a) be a party to, or otherwise interested in, any transaction or arrangement with the Company or in which the Company is otherwise (directly or indirectly) interested;

(b) act by himself or through his firm in a professional capacity for the Company (otherwise than as auditor) and he or his firm shall be entitled to remuneration for professional services as if he were not a Director;

(c) be or become a director or other officer of, or employed by, or a party to a transaction or arrangement with, or otherwise interested in, any body corporate in which the Company is otherwise (directly or indirectly) interested; and

(d) hold any office or place of profit with the Company (except as auditor) in conjunction with his office of Director for such period and upon such terms, including as to remuneration as the Board may decide.

110.2 A Director shall not, save as he may otherwise agree, be accountable to the Company for any benefit which he derives from any such contract, transaction or arrangement or from any such office or employment or from any interest in any such body corporate and no such contract, transaction or arrangement shall be liable to be avoided on the grounds of any such interest or benefit nor shall the receipt of any such remuneration or other benefit constitute a breach of his duty under section 176 of the Act.

111 **Authorisation of Directors' Conflicts of Interest**

111.1 The Board may, in accordance with the requirements set out in this Article, authorise any matter or situation proposed to them by any Director which would, if not authorised, involve a Director (an **Interested Director**) breaching his duty under the Act to avoid conflicts of interest.

111.2 A Director seeking authorisation in respect of a conflict of interest shall declare to the Board the nature and extent of his interest in a conflict of interest as soon as is reasonably practicable. The Director shall provide the Board with such details of the matter as are necessary for the Board to decide how to address the conflict of interest together with such additional information as may be requested by the Board.

111.3 Any authorisation under this Article will be effective only if:

(a) to the extent permitted by the Act, the matter in question shall have been proposed by any Director for consideration in the same way that any other matter may be proposed to the Directors under the provisions of these Articles;

(b) any requirement as to the quorum for consideration of the relevant matter is met without counting the Interested Director and any other interested Director; and

(c) the matter is agreed to without the Interested Director voting or would be agreed to if the Interested Director's and any other interested Director's vote is not counted.

111.4 Any authorisation of a conflict of interest under this Article must be recorded in writing (but the authority shall be effective whether or not the terms are so recorded) and may (whether at the time of giving the authorisation or subsequently):

(a) extend to any actual or potential conflict of interest which may reasonably be expected to arise out of the matter or situation so authorised;

(b) provide that the Interested Director be excluded from the receipt of documents and information and the participation in discussions (whether at meetings of the Directors or otherwise) related to the conflict of interest;

(c) impose upon the Interested Director such other terms for the purposes of dealing with the conflict of interest as the Directors think fit;

(d) provide that, where the Interested Director obtains, or has obtained (through his involvement in the conflict of interest and otherwise than through his position as a Director) information that is confidential to a third party, he will not be obliged to disclose that information to the Company, or to use it in relation to the

Company's affairs where to do so would amount to a breach of that confidence; and

(e) permit the Interested Director to absent himself from the discussion of matters relating to the conflict of interest at any meeting of the Directors and be excused from reviewing papers prepared by, or for, the Directors to the extent they relate to such matters.

111.5 Where the Directors authorise a conflict of interest, the Interested Director will be obliged to conduct himself in accordance with any terms and conditions imposed by the Directors in relation to the conflict of interest.

111.6 The Directors may revoke or vary such authorisation at any time, but this will not affect anything done by the Interested Director, prior to such revocation or variation, in accordance with the terms of such authorisation.

111.7 A Director is not required, by reason of being a Director (or because of the fiduciary relationship established by reason of being a director), to account to the Company for any remuneration, profit or other benefit which he derives from or in connection with a relationship involving a conflict of interest which has been authorised by the directors or by the Company in general meeting (subject in each case to any terms, limits or conditions attaching to that authorisation) and no contract shall be liable to be avoided on such grounds.

112 **Directors' Permitted Interests**

112.1 A Director cannot vote or be counted in the quorum on any resolution relating to any transaction or arrangement with the Company in which he has an interest and which may reasonably be regarded as likely to give rise to a conflict of interest but can vote (and be counted in the quorum) on the following:

(a) giving him any security, guarantee or indemnity for any money or any liability which he, or any other person, has lent or obligations he or any other person has undertaken at the request, or for the benefit, of the Company or any of its subsidiary undertakings;

(b) giving any security, guarantee or indemnity to any other person for a debt or obligation which is owed by the Company or any of its subsidiary undertakings, to that other person if the Director has taken responsibility for some or all of that debt or obligation. The Director can take this responsibility by giving a guarantee, indemnity or security;

(c) a proposal or contract relating to an offer of any shares or debentures or other securities for subscription or purchase by the Company or any of its subsidiary undertakings, if the Director takes part because he is a holder of shares, debentures or other securities, or if he takes part in the underwriting or sub-underwriting of the offer;

(d) any arrangement for the benefit of employees of the Company or any of its subsidiary undertakings which only gives him benefits which are also generally given to employees to whom the arrangement relates;

(e) any arrangement involving any other company if the Director (together with any person connected with the Director) has an interest of any kind in that company (including an interest by holding any position in that company or by being a shareholder of that company). This does not apply if he knows that he has a Relevant Interest;

(f) a contract relating to insurance which the Company can buy or renew for the benefit of the Directors or a group of people which includes Directors; and

(g) a contract relating to a pension, superannuation or similar scheme or a retirement, death, disability benefits scheme or employees' share scheme which gives the Director benefits which are also generally given to the employees to whom the scheme relates.

112.2 A Director cannot vote or be counted in the quorum on a resolution relating to his own appointment or the settlement or variation of the terms of his appointment to an office or place of profit with the Company or any other company in which the Company has an interest.

112.3 Where the Directors are considering proposals about the appointment, or the settlement or variation of the terms or the termination of the appointment of two or more Directors to other offices or places of profit with the Company or any company in which the Company has an interest, a separate resolution may be put in relation to each Director and in that case each of the Directors concerned shall be entitled to vote and be counted in the quorum in respect of each resolution unless it concerns his own appointment or the settlement or variation of the terms or the termination of his own appointment or the appointment of another director to an office or place of profit with a company in which the Company has an interest and the Director seeking to vote or be counted in the quorum has a Relevant Interest in it.

112.4 A company shall be deemed to be one in which the Director has a **Relevant Interest** if and so long as (but only if and so long as) he is to his knowledge (either directly or indirectly) the holder of or beneficially interested in one per cent or more of any class of the equity share capital of that company (calculated exclusive of any shares of that class in that company held as treasury shares) or of the voting rights available to members of that company. In relation to an alternate Director, an interest of his appointor shall be treated as an interest of the alternate Director without prejudice to any interest which the alternate Director has otherwise. Where a company in which a Director has Relevant Interest is interested in a contract, he also shall be deemed interested in that contract.

112.5 If a question arises at a Board meeting about whether a Director (other than the chairman of the meeting) has an interest which is likely to give rise to a conflict of interest, or whether he can vote or be counted in the quorum, and the Director does not agree to abstain from voting on the issue or not to be counted in the quorum, the question must be referred to the chairman of the meeting. The chairman's ruling about the relevant Director is final and conclusive, unless the nature and extent of the Director's interests have not been fairly disclosed to the Directors. If the question arises about the chairman of the meeting, the question must be directed to the Directors. The chairman cannot vote on the question but can be counted in the quorum. The Directors' resolution about the chairman is final and conclusive, unless the nature and extent of the chairman's interests have not been fairly disclosed to the Directors.

113 **General**

113.1 For the purposes of Articles 110 to 112 inclusive (which shall apply equally to alternate Directors):

(a) An interest of a person who is connected (which word shall have the meaning given to it by section 252 of the Act) with a Director shall be treated as an interest of the Director.

(b) A contract includes references to any proposed contract and to any transaction or arrangement or proposed transaction or arrangement whether or not constituting a contract.

(c) A conflict of interest includes a conflict of interest and duty and a conflict of duties.

(d) Subject to the Companies Acts, the Company may by ordinary resolution suspend or relax the provisions of Articles 110 to 112 to any extent or ratify any contract not properly authorised by reason of a contravention of any of the provisions of Articles 110 to 112.

114 **Power of Attorney**

The Board may, by power of attorney or otherwise, appoint any person or persons to be the agent or attorney of the Company and may delegate to any such person or persons any of its powers, authorities and discretions (with power to sub-delegate), in each case for such purposes and for such time, on such terms (including as to remuneration) and conditions as it thinks fit. The Board may confer such powers either collaterally with, or to the exclusion of and in substitution for, all or any of the powers of the Board in that respect and may revoke, withdraw, alter or vary any of such powers.

115 **Exercise of Voting Power**

The Board may exercise or cause to be exercised the voting power conferred by the shares in any other company held or owned by the Company, or any power of appointment to be exercised by the Company, in such manner as it thinks fit (including the exercise of the voting power or power of appointment in favour of the appointment of any Director as a director or other officer or employee of such company or in favour of the payment of remuneration to the directors, officers or employees of such company).

116 **Provision for Employees on Cessation of Business**

The Board may, by resolution, sanction the exercise of the power to make provision for the benefit of persons employed or formerly employed by the Company or any of its subsidiary undertakings, in connection with the cessation or the transfer to any person of the whole or part of the undertaking of the Company or that subsidiary undertaking, but any such resolution shall not be sufficient for payments to or for the benefit of directors, former directors or shadow directors.

117 **Overseas Registers**

Subject to the Companies Acts, the Company may keep an overseas, local or other register and the Board may make and vary such regulations as it thinks fit respecting the keeping of any such register.

118 **Borrowing Powers**

118.1 Subject to these Articles and the Companies Acts, the Board may exercise all the powers of the Company to:

(a) borrow money;

(b) indemnify and guarantee;

(c) mortgage or charge all or any part of the undertaking, property and assets (present and future) and uncalled capital of the Company;

(d) create and issue debentures and other securities; and

(e) give security either outright or as collateral security for any debt, liability or obligation of the Company or of any third party.

118.2 For the purpose of this Article, **Group** means the Company and its subsidiary undertakings for the time being.

118.3 Borrowings shall be deemed to include the following except in so far as otherwise taken into account:

(a) the nominal amount of any issued and paid up share capital (other than equity share capital) of any subsidiary undertaking of the Company owned otherwise than by a member of the Group;

(b) the nominal amount of any other issued and paid up share capital and the principal amount of any debentures or borrowed moneys which is not at the relevant time beneficially owned by a member of the Group, the redemption or repayment of which is the subject of a guarantee or indemnity by a member of the Group or which any member of the Group may be required to buy;

(c) the principal amount of any debenture (whether secured or unsecured) of a member of the Group beneficially owned otherwise than by a member of the Group;

(d) the outstanding amount raised by acceptances by any bank or accepting house under any acceptance credit opened by or on behalf of any member of the Group; and

(e) the minority proportion of moneys borrowed by a member of the Group and owing to a partly-owned subsidiary undertaking.

118.4 Borrowings shall not include and shall be deemed not to include:

(a) borrowings incurred by any member of the Group for the purpose of repaying within six months of the borrowing the whole or any part (with or without premium) of any borrowings of that or other member of the Group then outstanding, pending their application for such purpose within such period;

(b) the minority proportion of moneys borrowed by a partly owned subsidiary undertaking and not owing to another member of the Group.

118.5 When the aggregate principal amount of borrowings required to be taken into account on any particular date is being ascertained, any particular borrowing then outstanding which is denominated or repayable in a currency other than sterling shall be notionally converted into sterling at the rate of exchange prevailing in London on the last business day before that date or, if it would result in a lower figure, at the rate of exchange prevailing in London on the last business day six months before that date. For these purposes the rate of exchange shall be taken to be the spot rate in London recommended by a London clearing bank, selected by the Board, as being the most appropriate rate for the purchase by the company of the currency in question for sterling on the day in question.

118.6 A certificate or report by the auditors of the Company as to the amount of any borrowings or to the effect that the limit imposed by this Article has not been or will not be exceeded at any particular time or times, shall be conclusive evidence of such amount or fact for the purposes of this Article. Nevertheless the Board may at any time rely on a bona fide estimate of the aggregate of the borrowings. If, in consequence, the limit on borrowings set out in this Article is inadvertently exceeded, the amount of borrowings equal to the excess may be disregarded for 90 days after the date on which by reason of a determination of the auditors of the Company or otherwise the Board becomes aware that such a situation has or may have arisen.

118.7 No person dealing with the Company or any of its subsidiary undertakings shall be concerned to see or enquire whether the said limit is observed and no debt incurred or security given in excess of such limit shall be invalid or ineffectual unless the lender or recipient of the security had, at the time the debt was incurred or security given, express notice that the said limit had been or would be exceeded.

119 **Power to Authenticate Documents**

119.1 Any Director, the Secretary or any person appointed by the Board for the purpose shall have power to authenticate any documents affecting the constitution of the Company and any resolution passed by the Company or the Board or any committee, and any books, records, documents and accounts relating to the business of the Company, and to certify copies or extracts as true copies or extracts. Where any books, records, documents or accounts are not at the Office, the local manager or other officer of the Company who has their custody shall be deemed to be a person appointed by the Board for this purpose. A document purporting to be a copy of a resolution, or an extract from the minutes of a meeting, of the Company or the Board or any committee which is so certified shall be conclusive evidence in favour of all persons dealing with the Company that such resolution has been duly passed or, as the case may be, that any minute so extracted is a true and accurate record of proceedings at a duly constituted meeting.

120 **Use of Seals**

120.1 The Board shall provide for the safe custody of the Seal. A Seal shall not be used without the authority of the Board or of a committee of the Board so authorised.

120.2 Subject as otherwise provided in these Articles, every document which is sealed using the Seal must be signed by at least one authorised person in the presence of a witness who attests the signature. An authorised person for this purpose is any Director, the Secretary or any other person authorised by the Directors for the purpose of signing documents to which the Seal is applied.

120.3 The Seal shall be used only for sealing securities issued by the Company and documents creating or evidencing securities so issued. Any such securities or documents sealed with the Seal shall not require to be signed unless the Board decides otherwise or the law otherwise requires.

120.4 The Board may decide who will sign an instrument to which a Seal is affixed (or in the case of a share certificate, on which the Seal may be printed) either generally or in relation to a particular instrument or type of instrument and may also determine either generally or in a particular case that a signature may be dispensed with or affixed by mechanical means.

121 **Declaration of Dividends**

Subject to the Act and these Articles, the Company may by ordinary resolution declare dividends to be paid to members according to their respective rights and interests in the profits of the Company. However, no dividend shall exceed the amount recommended by the Board.

122 **Interim Dividends**

Subject to the Act, the Board may declare and pay such interim dividends (including any dividend at a fixed rate) as appears to the Board to be justified by the profits of the Company available for distribution. If the Board acts in good faith, it shall not incur any liability to the holders of shares for any loss that they may suffer by the lawful payment of any interim dividend on any other class of shares ranking with or after those shares.

123 **Calculation and Currency of Dividends**

Except as provided otherwise by the rights attached to shares, all dividends:

(a) shall be declared and paid accordingly to the amounts paid up (otherwise than in advance of calls) on the shares on which the dividend is paid;

(b) shall be apportioned and paid proportionately to the amounts paid up on the shares during any portion or portions of the period in respect of which the dividend is paid, but if any share is issued on terms that it shall rank for dividend as from a particular date, it shall rank for dividend accordingly; and

(c) may be declared or paid in any currency. The Board may decide the rate of exchange for any currency conversions that may be required and how any costs involved are to be met.

124 **Amounts Due on Shares can be Deducted from Dividends**

The Board may deduct from any dividend or other money payable to any person on or in respect of a share all such sums as may be due from him to the Company on account of calls or otherwise in relation to the shares of the Company. Sums so deducted can be used to pay amounts owing to the Company in respect of the shares.

125 **Dividends Not in Cash**

The Board may, by ordinary resolution of the Company direct, or in the case of an interim dividend may without the authority of an ordinary resolution direct, that payment of any dividend declared may be satisfied wholly or partly by the distribution of assets, and in particular of paid up shares or debentures of any other company, or in any one or more of such ways. Where any difficulty arises regarding such distribution, the Board may settle it as it thinks fit. In particular, the Board may:

(a) issue fractional certificates (or ignore fractions);

(b) fix the value for distribution of such assets or any part of them and determine that cash payments may be made to any members on the footing of the values so fixed, in order to adjust the rights of members; and

(c) vest any such assets in trustees on trust for the person entitled to the dividend.

126 **No Interest on Dividends**

Unless otherwise provided by the rights attached to the share, no dividend or other monies payable by the Company or in respect of a share shall bear interest as against the Company.

127 **Method of Payment**

127.1 The Company may pay any dividend, interest or other sum payable in respect of a share in cash or by direct debit, bank transfer, cheque, dividend warrant, or money order or by any other method, including by electronic means, as the Board may consider appropriate. For uncertificated shares, any payment may be made by means of the relevant system (subject always to the facilities and requirements of the relevant system) and such payment may be made by the Company or any person on its behalf by sending an instruction to the operator of the relevant system to credit the cash memorandum account of the holder or joint holders of such shares or, if permitted by the Company, of such person as the holder or joint holders may in writing direct.

127.2 The Company may send such payment by post or other delivery service (or by such means offered by the Company as the member or person entitled to it may agree in writing) to the registered address of the member or person entitled to it (or, if two or more persons are holders of the share or are jointly entitled to it because of the death or bankruptcy of the member or otherwise by operation of law, to the registered address of such of those persons as is first named in the Register) or to such person and such address as such member or person may direct in writing.

127.3 Every cheque, warrant, order or other form of payment is sent at the risk of the person entitled to the money represented by it, shall be made payable to the person or persons entitled, or to such other person as the person or persons entitled may direct in writing. Payment of the cheque, warrant, order or other form of payment (including transmission of funds through a bank transfer or other funds transfer system or by such other electronic means as permitted by these Articles or in accordance with the facilities and requirements of the relevant system concerned) shall be good discharge to the Company. If any such cheque, warrant, order or other form of payment has or shall be alleged to have been lost, stolen or destroyed the Company shall not be responsible.

127.4 Any joint holder or other person jointly entitled to a share may give an effective receipt for any dividend or other monies payable in respect of such share.

127.5 If a holder (or joint holder) does not specify an address, or does not specify an account or such other details and in each case that information is necessary in order to make a payment of a dividend, interest or other sum by the means by which in accordance with this Article the Board have decided that a payment is to be made or by which the holder (or joint holder) has validly elected to receive payment or the payment cannot be made by the Company using the details provided by the holder (or joint holders), the dividend, interest or other sum shall be treated as unclaimed for the purposes of these Articles.

127.6 The Board may, at its discretion, make provisions to enable any member as the Board shall determine to receive duly declared dividends in a currency or currencies other than sterling. For the purposes of the calculation of the amount receivable in respect of any dividend, the rate of exchange to be used to determine the foreign currency equivalent of any sum payable as a dividend shall be such rate or rates and the payment shall be on such terms and conditions as the Board may in its absolute discretion determine.

128 **Uncashed Dividends**

If cheques, warrants or orders for dividends or other sums payable in respect of a share sent by the Company to the person entitled to them are returned to the Company or left uncashed on two consecutive occasions or, following one occasion, reasonable enquires have failed to establish any new address to be used for the purpose, the Company does not have to send any dividends or other monies payable in respect of that share due to that person until he notifies the Company of an address to be used for the purpose.

129 **Unclaimed Dividends**

All dividends, interest or other sums payable and unclaimed for 12 months after having become payable may be invested or otherwise made use of by the Board for the benefit of the Company until claimed. The Company shall not be a trustee in respect of such unclaimed dividends and will not be liable to pay interest on it. All dividends that remain unclaimed for 12 years after they were first declared or became due for payment shall (if the Board so resolves) be forfeited and shall cease to remain owing by the Company.

130 **Scrip Dividends**

Subject to the Act, the Board may, by ordinary resolution of the Company and subject to such terms and conditions as the Board may determine, offer to any holders of ordinary shares

(excluding any member holding shares as treasury shares) the right to elect to receive ordinary shares, credited as fully paid, instead of cash in respect of the whole (or some part, to be determined by the Board) of any dividend specified by the ordinary resolution. The following provisions shall apply:

(a) the said resolution may specify a particular dividend, or may specify all or any dividends declared within a specified period or periods but such period may not end later than the fifth anniversary of the date of the meeting at which the ordinary resolution is passed;

(b) the entitlement of each holder of ordinary shares to new ordinary shares shall be such that the relevant value of the entitlement shall be as nearly as possible equal to (but not greater than) the cash amount (disregarding any tax credit) of the dividend that such holder would have received by way of dividend. For this purpose **relevant value** shall be calculated by reference to the average of the middle market quotations for the ordinary shares, certificated or uncertificated depositary instruments in respect of such shares, on NASDAQ (or any other publication of a recognised investment exchange showing quotations for the Company's ordinary shares), for the day on which the ordinary shares are first quoted "ex" the relevant dividend and the four subsequent dealing days, or in such other manner as the Board may determine on such basis as it considers to be fair and reasonable. A certificate or report by the Company's auditors as to the amount of the relevant value in respect of any dividend shall be conclusive evidence of that amount;

(c) no fractions of a share shall be allotted. The Board may make such provisions as it thinks fit for any fractional entitlements including provisions where, in whole or in part, the benefit accrues to the Company and/or under which fractional entitlements are accrued and/or retained and in each case accumulated on behalf of any member and such accruals or retentions are applied to the allotment by way of bonus to or cash subscription on behalf of any member of fully paid ordinary shares and/or provisions where cash payments may be made to members in respect of their fractional entitlements;

(d) the Board shall, after determining the basis of allotment, notify the holders of ordinary shares in writing of the right of election offered to them, and specify the procedure to be followed and place at which, and the latest time by which, elections must be lodged in order to be effective. No such notice need to be given to holders of ordinary shares who have previously given election mandates in accordance with this Article and whose mandates have not been revoked. The accidental omission to give notice of any right of election to, or the non-receipt (even if the Company becomes aware of such non-receipt) of any such notice by, any holder of ordinary shares entitled to the same shall neither invalidate any offer of an election nor give rise to any claim, suit or action;

(e) the Board shall not proceed with any election unless the company has sufficient reserves or funds that may be capitalised, and the Board has authority to allot sufficient shares, to give effect to it after the basis of the allotment is determined;

(f) the Board may exclude from any offer or make other arrangements in relation to any holders of ordinary shares where the Board considers that the making of the offer to them or in respect of such shares would or might involve the contravention of the laws of any territory or that for any other reason the offer should not be made to them or in respect of such shares;

(g) the Board may establish or vary a procedure for election mandates in respect of future rights of election and may determine that every duly effected election in respect of any ordinary shares shall be binding on every successor in title to the holder;

(h) the dividend (or that part of the dividend in respect of which a right of election has been offered) shall not be payable on ordinary shares in respect of which an election has been duly made (**elected ordinary shares**) and instead additional ordinary shares shall be allotted to the holders of the elected ordinary shares on the basis of allotment determined as stated above. For such purpose the Board may capitalise, out of any amount for the time being standing to the credit of any reserve or fund (including any share premium account or capital redemption reserve) or of any of the profits which could otherwise have been applied in paying dividends in cash as the Board may determine, a sum equal to the aggregate nominal amount of the additional ordinary shares to be allotted on such basis and apply it in paying up in full the appropriate number of unissued ordinary shares for allotment and distribution to the holders of the elected ordinary shares on such basis. The Board may do all acts and things considered necessary or expedient to give effect to any such capitalisation;

(i) the Board may decide how any costs relating to the new shares available in place of a cash dividend will be met, including to deduct an amount from the entitlement of a holder of ordinary shares under this Article;

(j) the additional ordinary shares so allotted shall rank pari passu in all respects with each other and with the fully paid ordinary shares in issue on the record date for the dividend in respect of which the right of election has been offered, except that they will not rank for any dividend or other distribution or other entitlement which has been declared, paid or made by reference to such record date; and

(k) the Board may terminate, suspend, or amend any offer of the right to elect to receive ordinary shares in lieu of any cash dividend at any time and generally may implement any scrip dividend scheme on such terms and conditions as the Board may determine and take such other action as the Board may deem necessary or desirable in respect of any such scheme.

131 **Capitalisation of Reserves**

131.1 The Board may, with the authority of an ordinary resolution of the Company:

(a) subject as provided in this Article, resolve to capitalise any undivided profits of the Company not required for paying any preferential dividend (whether or not they are available for distribution) or any sum standing to the credit of any reserve or fund of the Company which is available for distribution or standing to the credit of the share premium account or capital redemption reserve or other undistributable reserve;

(b) appropriate the sum resolved to be capitalised to the members in proportion to the nominal amounts of the shares (whether or not fully paid) held by them respectively which would entitle them to participate in a distribution of that sum if the shares were fully paid and the sum were then distributable and were distributed by way of dividend and apply such sum on their behalf either in or towards paying up the amounts, if any, for the time being unpaid on any shares held by them respectively, or in paying up in full unissued shares or debentures of the Company of a nominal amount equal to that sum, and allot the shares or debentures credited as fully paid to those members or as they may direct, in those proportions, or partly in one way and partly in the other, provided that:

(i) the share premium account, the capital redemption reserve, any other undistributable reserve and any profits which are not available for distribution may, for the purposes of this Article, only be applied in paying up in full shares to be allotted to members credited as fully paid;

(ii) the Company will also be entitled to participate in the relevant distribution in relation to any shares of the relevant class held by it as treasury shares and

the proportionate entitlement of the relevant class of members to the distribution will be calculated accordingly; and

(iii) in a case where any sum is applied in paying amounts for the time being unpaid on any shares of the Company or in paying up in full debentures of the Company, the amount of the net assets of the Company at that time in not less than the aggregate of the called up share capital of the Company and its undistributable reserves as shown in the latest audited accounts of the Company or such other accounts as may be relevant and would not be reduced below that aggregate by the payment of it;

(c) resolve that any shares so allotted to any member in respect of a holding by him of any partly paid shares shall, so long as such shares remain partly paid, rank for dividends only to the extent that such partly paid shares rank for dividends;

(d) make such provision by the issue of fractional certificates (or by ignoring fractions or by accruing the benefit of it to the Company rather than to the members concerned) or by payment in cash or otherwise as it thinks fit in the case of shares or debentures becoming distributable in fractions;

(e) authorise any person to enter on behalf of such members concerned into an agreement with the Company providing for either:

(i) the allotment to them respectively, credited as fully paid up, of any shares or debentures to which they may be entitled on such capitalisation; or

(ii) the payment up by the Company on behalf of such members by the application of their respective proportions of the reserves or profits resolved to be capitalised, of the amounts or any part of the amounts remaining unpaid on their existing shares,

(any agreement made under such authority being effective and binding on all such members); and

(f) generally do all acts and things required to give effect to such resolution.

132 **Record Dates**

132.1 Notwithstanding any other provision of these Articles but without prejudice to the rights attached to any shares and subject always to the Act, the Company or the Board may by resolution specify any date (**record date**) as the date at the close of business (or such other time as the Board may determine) on which persons registered as the holders of shares or other securities shall be entitled to receipt of any dividend, distribution, interest, allotment, issue, notice, information, document or circular. Such record date may be before, on or after the date on which the dividend, distribution, interest, allotment, issue, notice, information, document or circular is declared, made, paid, given, or served.

132.2 In the absence of a record date being fixed, entitlement to any dividend, distribution, interest, allotment, issue, notice, information, document or circular shall be determined by reference to the date on which the dividend is declared, the distribution allotment or issue is made or the notice, information, document or circular made, given or served.

133 **Inspection of Records**

No member (other than a Director) shall have any right to inspect any accounting record or other document of the Company unless he is authorised to do so by law, by order of a court of competent jurisdiction, by the Board or by ordinary resolution of the Company.

134 **Accounts to be Sent to Members**

134.1 In respect of each financial year, a copy of the Company's annual accounts, the strategic report, the Directors' report, the Directors' remuneration report, the auditor's report on those accounts and on the auditable part of the Directors' remuneration report shall be sent or supplied to:

(a) every member (whether or not entitled to receive notices of general meetings);

(b) every holder of debentures (whether or not entitled to receive notice of general meetings); and

(c) every other person who is entitled to receive notice of general meetings;

not less than 21 clear days before the date of the meeting at which copies of those documents are to be laid in accordance with the Act.

134.2 This Article does not require copies of the documents to which it applies to be sent or supplied to:

(a) a member or holder of debentures of whose address the Company is unaware; or

(b) more than one of the joint holders of shares or debentures.

134.3 The Board may determine that persons entitled to receive a copy of the Company's annual accounts, the strategic report, the Directors' report, the Directors' remuneration report, the auditor's report on those accounts and on the auditable part of the Directors' remuneration report are those persons entered on the Register at the close of business on a day determined by the Board, provided that the day determined by the Board may not be more than 21 days before the day that the relevant copies are being sent.

134.4 Where permitted by the Act, a strategic report with supplementary material in the form and containing the information prescribed by the Act may be sent or supplied to a person so electing in place of the documents required to be sent or supplied by Article 134.1.

135 **Service of Notices**

135.1 The Company can send, deliver or serve any notice or other document, including a share certificate, to or on a member:

(a) personally;

(b) by sending it through the postal system addressed to the member at his registered address or by leaving it at that address addressed to the member;

(c) through a relevant system, where the notice or document relates to uncertificated shares;

(d) where appropriate, by sending or supplying it in electronic form to an address notified by the member to the Company for that purpose;

(e) where appropriate, by making it available on a website and notifying the member of its availability in accordance with this Article; or

(f) by any other means authorised in writing by the member.

135.2 In the case of joint holders of a share:

(a) service, sending or supply of any notice, document or other information on or to one of the joint holders shall for all purposes be deemed a sufficient service on, sending or supplying to all the joint holders; and

(b) anything to be agreed or specified in relation to any notice, document or other information to be served on, sent or supplied to them may be agreed or specified by any one of the joint holders and the agreement or specification of the first named in the Register shall be accepted to the exclusion of that of the other joint holders.

135.3 Where a member (or, in the case of a joint holders, the person first named in the Register) has a registered address outside the United Kingdom but has notified the Company of an address within the United Kingdom at which notices, documents or other information may be given to him or has given to the Company an address for the purposes of communications by electronic means at which notices, documents or other information may be served, sent or supplied to him, the member shall be entitled to have notices served, sent or supplied to him at such address or, where applicable, the Company may make them available on a website and notify the holder of that address. Otherwise no such member shall be entitled to receive any notice, document or other information from the Company.

135.4 If on three consecutive occasions any notice, document or other information has been sent to any member at the member's registered address or the member's address for the service of notices (by electronic means or otherwise) but has been returned undelivered, such member shall not be entitled to receive notices, documents or other information from the Company until he shall have communicated with the Company and supplied in writing a new registered address or address within the United Kingdom for the service of notices or has informed the Company of an address for the service of notices and the sending or supply of documents and other information in electronic form. For these purposes, any notice, document or other information served, sent or supplied by post shall be treated as returned undelivered if the notice, document or other information is served, sent or supplied back to the Company (or its agents) and a notice, document or other information served, sent or supplied in electronic form shall be treated as returned undelivered if the Company (or its agents) receives notification that the notice, document or other information was not delivered to the address to which it was served, sent or supplied.

135.5 The Company may at any time and in its sole discretion choose to serve, send or supply notices, documents or other information in hard copy form alone to some or all of the members.

136 **Notice on Person Entitled By Transmission**

The Company may give notice to the person entitled to a share because of the death or bankruptcy of a member or otherwise by operation of law, by sending or delivering it in any manner authorised by these Articles for the giving of notice to a member, addressed to that person by name, or by the title of representative of the deceased or trustee of the bankrupt or representative by operation of law or by any like description, at the address (if any) within the United Kingdom supplied for the purpose by the person claimed to be so entitled or to which notices may be sent in electronic form. Until such an address has been so supplied, a notice may be given in any manner in which it might have been given if the death or bankruptcy or operation of law had not occurred.

137 **Record Date for Service**

Any notice, document or other information may be served, sent or supplied by the Company by reference to the register as it stands at any time not more than 15 days before the date of service, sending or supplying. No change in the register after that time shall invalidate that service, sending or supply. Where any notice, document or other information is served on, sent or supplied to any person in respect of a share in accordance with these Articles, no

person deriving any title or interest in that share shall be entitled to any further service, sending or supplying of that notice, document or other information.

138 **Evidence of Service**

138.1 Any notice, document or other information, addressed to a member at the member's registered address or address for service in the United Kingdom shall, if served, sent or supplied by first class post, be deemed to have been served or delivered on the day after the day when it was put in the post (or, where second class post is employed, on the second day after the day when it was put in the post). Proof that an envelope containing the notice, document or other information was properly addressed and put into the post as a prepaid letter shall be conclusive evidence that the notice was given.

138.2 Any notice, document or other information not served, sent or supplied by post but delivered or left at a registered address or address for service in the United Kingdom (other than an address for the purposes of communications by electronic means) shall be deemed to have been served or delivered on the day on which it was so delivered or left.

138.3 Any notice, document or other information, if served, sent or supplied by electronic means shall be deemed to have been received on the day on which the electronic communication was sent by or on behalf of the Company notwithstanding that the Company subsequently sends a hard copy of such notice, document or other information by post. Any notice, document or other information made available on a website shall be deemed to have been received on the day on which the notice, document or other information was first made available on the website or, if later, when a notice of availability is received or deemed to have been received pursuant to this Article. Proof that the notice, document or other information was properly addressed shall be conclusive evidence that the notice by electronic means was given.

138.4 Any notice, document or other information served, sent or supplied by the Company by means of a relevant system shall be deemed to have been received when the Company or any sponsoring system-participant acting on its behalf sends the issuer instruction relating to the notice, document or other information.

138.5 Any notice, document or other information served, sent or supplied by the Company by any other means authorised in writing by the member concerned shall be deemed to have been received when the Company has carried out the action it has been authorised to take for that purpose.

139 **Notice When Post not Available**

If at any time by reason of the suspension, interruption or curtailment of postal services within the United Kingdom the Company is unable effectively to convene a general meeting by notices sent through the post, the Company need only give notice of a general meeting to those members with whom the Company can communicate by electronic means and who have provided the Company with an address for this purpose. The Company shall also advertise the notice in at least one national newspaper published in the United Kingdom and make it available on its website from the date of such advertisement until the conclusion of the meeting or any adjournment of it. In any such case the Company shall send confirmatory copies of the notice by post to those members to whom notice cannot be given by electronic means if, at least seven days prior to the meeting, the posting of notices to addresses throughout the United Kingdom again becomes practicable.

140 **Indemnity and Insurance**

140.1 In this Article:

(a) companies are **associated** if one is a subsidiary of the other or both are subsidiaries of the same body corporate;

(b) a **relevant officer** means any Director or other officer or former director or other officer of the Company or an associated company (including any company which is a trustee of an occupational pension scheme (as defined by section 235(6) of the Act), but excluding in each case any person engaged by the Company (or associated company) as auditor (whether or not he is also a director or other officer), to the extent he acts in his capacity as auditor); and

(c) **relevant loss** means any loss or liability which has been or may be incurred by a relevant officer in connection with that relevant officer's duties or powers in relation to the company, any associated company or any pension fund or employees' share scheme of the company or associated company.

140.2 Subject to Article 140.4, but without prejudice to any indemnity to which a relevant officer is otherwise entitled:

(a) each relevant officer shall be indemnified out of the Company's assets against all relevant loss and in relation to the Company's (or any associated company's) activities as trustee of an occupational pension scheme (as defined in section 235(6) of the Act), including any liability incurred by him in defending any civil or criminal proceedings, in which judgment is given in his favour or in which he is acquitted or the proceedings are otherwise disposed of without any finding or admission of any material breach of duty on his part or in connection with any application in which the court grants him, in his capacity as a relevant officer, relief from liability for negligence, default, breach of duty or breach of trust in relation to the Company's (or any associated company's) affairs; and

(b) the Company may provide any relevant officer with funds to meet expenditure incurred or to be incurred by him in connection with any proceedings or application referred to in Article 140.2(a) and otherwise may take any action to enable any such relevant officer to avoid incurring such expenditure.

140.3 This Article does not authorise any indemnity which would be prohibited or rendered void by any provision of the Companies Acts or by any other provision of law.

140.4 The Directors may decide to purchase and maintain insurance, at the expense of the Company, for the benefit of any relevant officer in respect of any relevant loss.

141 **Winding Up**

141.1 If the Company is wound up, the liquidator may, with the authority of a special resolution and any other authority required by law, divide among the members in specie the whole or any part of the assets of the Company. This applies whether the assets shall consist of property of one kind or different kinds. For this purpose, the liquidator may set such value as the liquidator considers fair on any asset or assets and may determine how to divide it between the members or different classes of members. The liquidator may, with the authority of a special resolution and any other authority required by the law, transfer all or any part of the assets to trustees on such trusts for the benefit of members as the liquidator decides. Where the liquidator divides or transfers any assets in pursuance of the powers in this Article, no member shall be required to accept any asset in respect of which there is a liability.

141.2 Article 141.1 is without prejudice to any right or power that the liquidator may have, in the absence of the rights expressly conferred by Article 141.1, to divide or transfer the assets in specie as contemplated in Article 141.1 without a special resolution.

Exhibit 4.1

DEPOSIT AGREEMENT

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by and among

BICYCLE THERAPEUTICS PLC

and

CITIBANK, N.A.,
as Depositary,

and

THE HOLDERS AND BENEFICIAL OWNERS OF
AMERICAN DEPOSITARY SHARES
ISSUED HEREUNDER

Dated as of **[date]**, 2019

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DEPOSIT AGREEMENT

DEPOSIT AGREEMENT, dated as of , 2019, by and among (i) Bicycle Therapeutics plc, a public limited company incorporated under the laws of England and Wales, and its successors (the "Company"), (ii) CITIBANK, N.A., a national banking association organized under the laws of the United States of America ("Citibank") acting in its capacity as depositary, and any successor depositary hereunder (Citibank in such capacity, the "Depositary"), and (iii) all Holders and Beneficial Owners of American Depositary Shares issued hereunder (all such capitalized terms as hereinafter defined).

W I T N E S S E T H T H A T:

WHEREAS, the Company desires to establish with the Depositary an ADR facility to provide for the deposit of the Shares (as hereinafter defined) and the creation of American Depositary Shares representing the Shares so deposited and for the execution and Delivery (as hereinafter defined) of American Depositary Receipts (as hereinafter defined) evidencing such American Depositary Shares; and

WHEREAS, the Depositary is willing to act as the Depositary for such ADR facility upon the terms set forth in the Deposit Agreement (as hereinafter defined); and

WHEREAS, any American Depositary Receipts issued pursuant to the terms of the Deposit Agreement are to be substantially in the form of Exhibit A attached hereto, with appropriate insertions, modifications and omissions, as hereinafter provided in the Deposit Agreement; and

WHEREAS, the Board of Directors of the Company (or an authorized committee thereof) has duly approved the establishment of an ADR facility upon the terms set forth in the Deposit Agreement, the execution and delivery of the Deposit Agreement on behalf of the Company, and the actions of the Company and the transactions contemplated hereby.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

ARTICLE I

DEFINITIONS

All capitalized terms used, but not otherwise defined, herein shall have the meanings set forth below, unless otherwise clearly indicated:

Section 1.1 "**ADS Record Date**" shall have the meaning given to such term in Section 4.9.

Section 1.2 **"Affiliate"** shall have the meaning assigned to such term by the Commission (as hereinafter defined) under Regulation C promulgated under the Securities Act (as hereinafter defined), or under any successor regulation thereto.

Section 1.3 "**American Depositary Receipt(s)**", "**ADR(s)**" and "**Receipt(s)**" shall mean the certificate(s) issued by the Depositary to evidence the American Depositary Shares issued under the terms of the Deposit Agreement in the form of Certificated ADS(s) (as hereinafter defined), as such ADRs may be amended from time to time in accordance with the provisions of the Deposit Agreement. An ADR may evidence any number of ADSs and may, in the case of ADSs held through a central depository such as DTC, be in the form of a "Balance Certificate."

Section 1.4 "**American Depositary Share(s)**" and "**ADS(s)**" shall mean the rights and interests in the Deposited Property (as hereinafter defined) granted to the Holders and Beneficial Owners pursuant to the terms and conditions of the Deposit Agreement and, if issued as Certificated ADS(s) (as hereinafter defined), the ADR(s) issued to evidence such ADSs. ADS(s) may be issued under the terms of the Deposit Agreement in the form of (a) Certificated ADS(s) (as hereinafter defined), in which case the ADS(s) are evidenced by ADR(s), or (b) Uncertificated ADS(s) (as hereinafter defined), in which case the ADS(s) are not evidenced by ADR(s) but are reflected on the direct registration system maintained by the Depositary for such purposes under the terms of Section 2.13. Unless otherwise specified in the Deposit Agreement or in any ADR, or unless the context otherwise requires, any reference to ADS(s) shall include Certificated ADS(s) and Uncertificated ADS(s), individually or collectively, as the context may require. Each ADS shall represent the right to receive, and to exercise the beneficial ownership interests in, the number of Shares specified in the form of ADR attached hereto as Exhibit A (as amended from time to time) that are on deposit with the Depositary and/or the Custodian, subject, in each case, to the terms and conditions of the Deposit Agreement and the applicable ADR (if issued as a Certificated ADS), until there shall occur a distribution upon Deposited Securities referred to in Section 4.2 or a change in Deposited Securities referred to in Section 4.11 with respect to which additional ADSs are not issued, and thereafter each ADS shall represent the right to receive, and to exercise the beneficial ownership interests in, the applicable Deposited Property on deposit with the Depositary and the Custodian determined in accordance with the terms of such Sections, subject, in each case, to the terms and conditions of the Deposit Agreement and the applicable ADR (if issued as a Certificated ADS). In addition, the ADS(s)-to-Share(s) ratio is subject to amendment as provided in Articles IV and VI of the Deposit Agreement (which may give rise to Depositary fees).

Section 1.5 "**Applicant**" shall have the meaning given to such term in Section 5.10.

Section 1.6 "**Articles of Association**" shall mean the Articles of Association of the Company, as amended and restated from time to time.

Section 1.7 "**Beneficial Owner**" shall mean, as to any ADS, any person or entity having a beneficial interest deriving from the ownership of such ADS. Notwithstanding anything else contained in the Deposit Agreement, any ADR(s) or any other instruments or agreements relating to the ADSs and the corresponding Deposited Property, the Depositary, the Custodian and their respective nominees are intended to be, and shall at all times during the term of the Deposit Agreement be, the record holders only of the Deposited Property represented by the ADSs for the benefit of the Holders and Beneficial Owners of the corresponding ADSs. The Depositary, on its own behalf and on behalf of the Custodian and their respective nominees,

disclaims any beneficial ownership interest in the Deposited Property held on behalf of the Holders and Beneficial Owners of ADSs. The beneficial ownership interests in the Deposited Property are intended to be, and shall at all times during the term of the Deposit Agreement continue to be, vested in the Beneficial Owners of the ADSs representing the Deposited Property. The beneficial ownership interests in the Deposited Property shall, unless otherwise agreed by the Depositary, be exercisable by the Beneficial Owners of the ADSs only through the Holders of such ADSs, by the Holders of the ADSs (on behalf of the applicable Beneficial Owners) only through the Depositary, and by the Depositary (on behalf of the Holders and Beneficial Owners of the corresponding ADSs) directly, or indirectly through the Custodian or their respective nominees, in each case upon the terms of the Deposit Agreement and, if applicable, the terms of the ADR(s) evidencing the ADSs. A Beneficial Owner of ADSs may or may not be the Holder of such ADSs. A Beneficial Owner shall be able to exercise any right or receive any benefit hereunder solely through the person who is the Holder of the ADSs owned by such Beneficial Owner. Unless otherwise identified to the Depositary, a Holder shall be deemed to be the Beneficial Owner of all the ADSs registered in his/her/its name. The manner in which a Beneficial Owner holds ADSs (e.g., in a brokerage account vs. as registered holder) may affect the rights and obligations of, the manner in which, and the extent to which, services are made available to, Beneficial Owners pursuant to the terms of the Deposit Agreement.

Section 1.8 **"Certificated ADS(s)"** shall have the meaning set forth in Section 2.13.

Section 1.9 **"Citibank"** shall mean Citibank, N.A., a national banking association organized under the laws of the United States of America, and its successors.

Section 1.10 "**Commission**" shall mean the Securities and Exchange Commission of the United States or any successor governmental agency thereto in the United States.

Section 1.11 "**Company**" shall mean Bicycle Therapeutics plc, a public limited company incorporated and existing under the laws of England and Wales, and its successors.

Section 1.12 "**CREST**" shall mean the system for the paperless settlement of trades in securities and the holding of uncertificated securities operated by CREST Limited in accordance with the Uncertificated Securities Regulations 2001 (SI 2001 No. 3755), as amended from time to time, or any successor thereto.

Section 1.13 "**Custodian**" shall mean (i) as of the date hereof, Citibank, N.A. (London), having its principal office at Citigroup Centre, Canary Wharf, London, E14 5LB, United Kingdom, as the custodian of Deposited Property for the purposes of the Deposit Agreement, (ii) Citibank, N.A., acting as custodian of Deposited Property pursuant to the Deposit Agreement, and (iii) any other entity that may be appointed by the Depositary pursuant to the terms of Section 5.5 as successor, substitute or additional custodian hereunder. The term "Custodian" shall mean any Custodian individually or all Custodians collectively, as the context requires.

Section 1.14 "**Deliver**" and "**Delivery**" shall mean (x) *when used in respect of Shares and other Deposited Securities*, whichever is appropriate of (i) the physical delivery of the

certificate(s) representing such securities, or (ii) the book-entry transfer and recordation of such securities on the books of the Share Registrar (as hereinafter defined) or in the book-entry settlement of CREST, and (y) *when used in respect of ADSs*, either (i) the physical delivery of ADR(s) evidencing the ADSs, or (ii) the book-entry transfer and recordation of ADSs on the books of the Depositary or any book-entry settlement system in which the ADSs are settlement-eligible.

Section 1.15 "**Deposit Agreement**" shall mean this Deposit Agreement and all exhibits hereto, as the same may from time to time be amended and supplemented from time to time in accordance with the terms of the Deposit Agreement.

Section 1.16 "**Depositary**" shall mean Citibank, N.A., a national banking association organized under the laws of the United States, in its capacity as depositary under the terms of the Deposit Agreement, and any successor depositary hereunder.

Section 1.17 **"Deposited Property"** shall mean the Deposited Securities and any cash and other property held on deposit by the Depositary and the Custodian in respect of the ADSs or the Deposited Securities under the terms of the Deposit Agreement, subject, in the case of cash, to the provisions of Section 4.8. All Deposited Property shall be held by the Custodian, the Depositary and their respective nominees for the benefit of the Holders and Beneficial Owners of the ADSs representing the Deposited Property. The Deposited Property is not intended to, and shall not, constitute proprietary assets of the Depositary, the Custodian or their nominees. Beneficial ownership in the Deposited Property is intended to be, and shall at all times during the term of the Deposit Agreement continue to be, vested in the Beneficial Owners of the ADSs representing the Deposited Property.

Section 1.18 **"Deposited Securities"** shall mean the Shares and any other securities held on deposit by the Custodian from time to time in respect of the ADSs under the Deposit Agreement and constituting Deposited Property.

Section 1.19 "**Dollars**" and "**$**" shall refer to the lawful currency of the United States.

Section 1.20 "**DTC**" shall mean The Depository Trust Company, a national clearinghouse and the central book-entry settlement system for securities traded in the United States and, as such, the custodian for the securities of DTC Participants (as hereinafter defined) maintained in DTC, and any successor thereto.

Section 1.21 "**DTC Participant**" shall mean any financial institution (or any nominee of such institution) having one or more participant accounts with DTC for receiving, holding and delivering the securities and cash held in DTC. A DTC Participant may or may not be a Beneficial Owner. If a DTC Participant is not the Beneficial Owner of the ADSs credited to its account at DTC, or of the ADSs in respect of which the DTC Participant is otherwise acting, such DTC Participant shall be deemed, for all purposes hereunder, to have all requisite authority to act on behalf of the Beneficial Owner(s) of the ADSs credited to its account at DTC or in respect of which the DTC Participant is so acting. A DTC Participant, upon acceptance in any one of its DTC accounts of any ADSs (or any interest therein) issued in accordance with the

terms and conditions of the Deposit Agreement, shall (notwithstanding any explicit or implicit disclosure that it may be acting on behalf of another party) be deemed for all purposes to be a party to, and bound by, the terms of the Deposit Agreement and the applicable ADR(s) to the same extent as, and as if the DTC Participant were, the Holder of such ADSs.

Section 1.22 "**Exchange Act**" shall mean the United States Securities Exchange Act of 1934, as amended from time to time.

Section 1.23 "**Foreign Currency**" shall mean any currency other than Dollars.

Section 1.24 **"Full Entitlement ADR(s)", "Full Entitlement ADS(s)" and "Full Entitlement Share(s)"** shall have the respective meanings set forth in Section 2.12.

Section 1.25 "**Holder(s)**" shall mean the person(s) in whose name the ADSs are registered on the books of the Depositary (or the Registrar, if any) maintained for such purpose. A Holder may or may not be a Beneficial Owner. If a Holder is not the Beneficial Owner of the ADS(s) registered in its name, such person shall be deemed, for all purposes hereunder, to have all requisite authority to act on behalf of the Beneficial Owners of the ADSs registered in its name. The manner in which a Holder holds ADSs (e.g., in certificated vs. uncertificated form) may affect the rights and obligations of, and the manner in which, and the extent to which, the services are made available to, Holders pursuant to the terms of the Deposit Agreement.

Section 1.26 **"Partial Entitlement ADR(s)", "Partial Entitlement ADS(s)" and "Partial Entitlement Share(s)"** shall have the respective meanings set forth in Section 2.12.

Section 1.27 "**Pounds**", "**Pence**", **and** "**£**" shall refer to the lawful currency of England.

Section 1.28 "**Principal Office**" shall mean, when used with respect to the Depositary, the principal office of the Depositary at which at any particular time its depositary receipts business shall be administered, which, at the date of the Deposit Agreement, is located at 388 Greenwich Street, New York, New York 10013, U.S.A.

Section 1.29 "**Registrar**" shall mean the Depositary or any bank or trust company having an office in the Borough of Manhattan, The City of New York, which shall be appointed by the Depositary to register issuances, transfers and cancellations of ADSs as herein provided, and shall include any co-registrar appointed by the Depositary for such purposes. Registrars (other than the Depositary) may be removed and substitutes appointed by the Depositary. Each Registrar (other than the Depositary) appointed pursuant to the Deposit Agreement shall be required to give notice in writing to the Depositary accepting such appointment and agreeing to be bound by the applicable terms of the Deposit Agreement.

Section 1.30 "**Restricted Securities**" shall mean Shares, Deposited Securities or ADSs which (i) have been acquired directly or indirectly from the Company or any of its Affiliates in a transaction or chain of transactions not involving any public offering and are subject to resale limitations under the Securities Act or the rules issued thereunder, or (ii) are held by an executive officer or director (or persons performing similar functions) or other Affiliate of the Company, or

(iii) are subject to other restrictions on sale or deposit under the laws of the United States, England and Wales, or under a shareholder agreement or the Articles of Association of the Company or under the regulations of an applicable securities exchange unless, in each case, such Shares, Deposited Securities or ADSs are being transferred or sold to persons other than an Affiliate of the Company in a transaction (a) covered by an effective resale registration statement, or (b) exempt from the registration requirements of the Securities Act (as hereinafter defined), and the Shares, Deposited Securities or ADSs are not, when held by such person(s), Restricted Securities.

Section 1.31 "**Restricted ADR(s)" "Restricted ADS(s)" and "Restricted Shares"** shall have the respective meanings set forth in Section 2.14.

Section 1.32 "**Securities Act**" shall mean the United States Securities Act of 1933, as amended from time to time.

Section 1.33 "**Share Registrar**" shall mean Computershare Investor Services plc, a company registered in England and Wales or any other institution organized under the laws of England and Wales appointed by the Company from time to time to carry out the duties of registrar for the Shares, and any successor thereto.

Section 1.34 "**Shares**" shall mean the Company's ordinary shares, with a nominal value of £0.01 per share, validly issued and outstanding and fully paid and may, if the Depositary so agrees after consultation with the Company, include evidence of the right to receive Shares; provided that in no event shall Shares include evidence of the right to receive Shares with respect to which the full purchase price has not been paid or Shares as to which preemptive rights have theretofore not been validly waived or exercised; provided further, however, that, if there shall occur any change in nominal value, split-up, consolidation, reclassification, exchange, conversion or any other event described in Section 4.11 in respect of the Shares of the Company, the term "Shares" shall thereafter, to the maximum extent permitted by law, represent the successor securities resulting from such event.

Section 1.35 **"Uncertificated ADS(s)"** shall have the meaning set forth in Section 2.13.

Section 1.36 "**United States**" and "**U.S.**" shall have the meaning assigned to it in Regulation S as promulgated by the Commission under the Securities Act.

ARTICLE II

APPOINTMENT OF DEPOSITARY; FORM OF RECEIPTS; DEPOSIT OF SHARES; EXECUTION AND DELIVERY, TRANSFER AND SURRENDER OF RECEIPTS

Section 2.1 **Appointment of Depositary.** The Company hereby appoints the Depositary as depositary for the Deposited Property and hereby authorizes and directs the Depositary to act in accordance with the terms and conditions set forth in the Deposit Agreement and the applicable ADRs. Each Holder and each Beneficial Owner, upon acceptance of any ADSs (or any interest therein) issued in accordance with the terms and conditions of the Deposit Agreement shall be deemed for all purposes to (a) be a party to and bound by the terms of the Deposit Agreement and the applicable ADR(s), and (b) appoint the Depositary its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in the Deposit Agreement and the applicable ADR(s), to adopt any and all procedures necessary to comply with applicable law and to take such action as the Depositary in its sole discretion may deem necessary or appropriate to carry out the purposes of the Deposit Agreement and the applicable ADR(s), the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof.

Section 2.2 **Form and Transferability of ADSs.**

(a) **Form.** Certificated ADSs shall be evidenced by definitive ADRs which shall be engraved, printed, lithographed or produced in such other manner as may be agreed upon by the Company and the Depositary. ADRs may be issued under the Deposit Agreement in denominations of any whole number of ADSs. The ADRs shall be substantially in the form set forth in Exhibit A to the Deposit Agreement, with any appropriate insertions, modifications and omissions, in each case as otherwise contemplated in the Deposit Agreement or required by law. ADRs shall be (i) dated, (ii) signed by the manual or facsimile signature of a duly authorized signatory of the Depositary, (iii) countersigned by the manual or facsimile signature of a duly authorized signatory of the Registrar, and (iv) registered in the books maintained by the Registrar for the registration of issuances and transfers of ADSs. No ADR and no Certificated ADS evidenced thereby shall be entitled to any benefits under the Deposit Agreement or be valid or enforceable for any purpose against the Depositary or the Company, unless such ADR shall have been so dated, signed, countersigned and registered. ADRs bearing the facsimile signature of a duly-authorized signatory of the Depositary or the Registrar, who at the time of signature was a duly-authorized signatory of the Depositary or the Registrar, as the case may be, shall bind the Depositary, notwithstanding the fact that such signatory has ceased to be so authorized prior to the Delivery of such ADR by the Depositary. The ADRs shall bear a CUSIP number that is different from any CUSIP number that was, is or may be assigned to any depositary receipts previously or subsequently issued pursuant to any other arrangement between the Depositary (or any other depositary) and the Company and which are not ADRs outstanding hereunder.

(b) **Legends.** The ADRs may be endorsed with, or have incorporated in the text thereof, such legends or recitals not inconsistent with the provisions of the Deposit Agreement as may be (i) necessary to enable the Depositary and the Company to perform their respective

obligations hereunder, (ii) required to comply with any applicable laws or regulations, or with the rules and regulations of any securities exchange or market upon which ADSs may be traded, listed or quoted, or to conform with any usage with respect thereto, (iii) necessary to indicate any special limitations or restrictions to which any particular ADRs or ADSs are subject by reason of the date of issuance of the Deposited Securities or otherwise, or (iv) required by any book-entry system in which the ADSs are held. Holders and Beneficial Owners shall be deemed, for all purposes, to have notice of, and to be bound by, the terms and conditions of the legends set forth, in the case of Holders, on the ADR registered in the name of the applicable Holders or, in the case of Beneficial Owners, on the ADR representing the ADSs owned by such Beneficial Owners.

(c) Title. Subject to the limitations contained herein and in the ADR, title to an ADR (and to each Certificated ADS evidenced thereby) shall be transferable upon the same terms as a certificated security under the laws of the State of New York, provided that, in the case of Certificated ADSs, such ADR has been properly endorsed or is accompanied by proper instruments of transfer. Notwithstanding any notice to the contrary, the Depositary and the Company may deem and treat the Holder of an ADS (that is, the person in whose name an ADS is registered on the books of the Depositary) as the absolute owner thereof for all purposes. Neither the Depositary nor the Company shall have any obligation nor be subject to any liability under the Deposit Agreement or any ADR to any holder or any Beneficial Owner unless, in the case of a holder of ADSs, such holder is the Holder registered on the books of the Depositary or, in the case of a Beneficial Owner, such Beneficial Owner, or the Beneficial Owner's representative, is the Holder registered on the books of the Depositary.

(d) Book-Entry Systems. The Depositary shall make arrangements for the acceptance of the ADSs into DTC. All ADSs held through DTC will be registered in the name of the nominee for DTC (currently "Cede & Co."). The nominee of DTC will be the only "Holder" of all ADSs held through DTC. Unless issued by the Depositary as Uncertificated ADSs, the ADSs registered in the name of Cede & Co. will be evidenced by one or more ADR(s) in the form of a "Balance Certificate," which will provide that it represents the aggregate number of ADSs from time to time indicated in the records of the Depositary as being issued hereunder and that the aggregate number of ADSs represented thereby may from time to time be increased or decreased by making adjustments on such records of the Depositary and of DTC or its nominee as hereinafter provided. Citibank, N.A. (or such other entity as is appointed by DTC or its nominee) may hold the "Balance Certificate" as custodian for DTC. Each Beneficial Owner of ADSs held through DTC must rely upon the procedures of DTC and the DTC Participants to exercise or be entitled to any rights attributable to such ADSs. The DTC Participants shall for all purposes be deemed to have all requisite power and authority to act on behalf of the Beneficial Owners of the ADSs held in the DTC Participants' respective accounts in DTC and the Depositary shall for all purposes be authorized to rely upon any instructions and information given to it by DTC Participants. So long as ADSs are held through DTC or unless otherwise required by law, ownership of beneficial interests in the ADSs registered in the name of the nominee for DTC will be shown on, and transfers of such ownership will be effected only through, records maintained by (i) DTC or its nominee (with respect to the interests of DTC Participants), or (ii) DTC Participants or their nominees (with respect to the interests of clients of DTC Participants). Any distributions made, and any notices given, by the Depositary to DTC

under the terms of the Deposit Agreement shall (unless otherwise specified by the Depositary) satisfy the Depositary's obligations under the Deposit Agreement to make such distributions, and give such notices, in respect of the ADSs held in DTC (including, for avoidance of doubt, to the DTC Participants holding the ADSs in their DTC accounts and to the Beneficial Owners of such ADSs).

Section 2.3 **Deposit of Shares.** Subject to the terms and conditions of the Deposit Agreement and applicable law, Shares or evidence of rights to receive Shares (other than Restricted Securities) may be deposited by any person (including the Depositary in its individual capacity but subject, however, in the case of the Company or any Affiliate of the Company, to Section 5.7) at any time, whether or not the transfer books of the Company or the Share Registrar, if any, are closed, by Delivery of the Shares to the Custodian. Every deposit of Shares shall be accompanied by the following: (A) (i) *in the case of Shares represented by certificates issued in registered form*, the certificate(s) representing such Shares and, where relevant, appropriate instruments of transfer or endorsement, in a form reasonably satisfactory to the Custodian, (ii) *in the case of Shares represented by certificates in bearer form*, the requisite coupons and talons pertaining thereto, and (iii) *in the case of Shares delivered by book-entry transfer and recordation*, confirmation of such book-entry transfer and recordation in the books of the Share Registrar or of CREST, as applicable, to the Custodian or that irrevocable instructions have been given to cause such Shares to be so issued or transferred, as applicable, and recorded, (B) such certifications and payments (including, without limitation, the Depositary's fees and related charges) and evidence of such payments (including, without limitation, stamping or otherwise marking such Shares by way of receipt) as may be reasonably required by the Depositary or the Custodian in accordance with the provisions of the Deposit Agreement and applicable law, (C) if the Depositary so requires, a written order directing the Depositary to issue and deliver to, or upon the written order of, the person(s) stated in such order the number of ADSs representing the Shares so deposited, (D) evidence reasonably satisfactory to the Depositary (which may be an opinion of counsel) that all necessary approvals have been granted by, or there has been compliance with the rules and regulations of, any applicable governmental agency in England and Wales, and (E) if the Depositary so requires, (i) an agreement, assignment or instrument reasonably satisfactory to the Depositary or the Custodian which provides for the prompt transfer by any person in whose name the Shares are or have been recorded to the Custodian of any distribution, or right to subscribe for additional Shares or to receive other property in respect of any such deposited Shares or, in lieu thereof, such indemnity or other agreement as shall be reasonably satisfactory to the Depositary or the Custodian and (ii) if the Shares are registered in the name of the person on whose behalf they are presented for deposit, a proxy or proxies entitling the Custodian to exercise voting rights in respect of the Shares for any and all purposes until the Shares so deposited are registered in the name of the Depositary, the Custodian or any nominee.

Without limiting any other provision of the Deposit Agreement, the Depositary shall instruct the Custodian not to, and the Depositary shall not knowingly, accept for deposit (a) any Restricted Securities (except as contemplated by Section 2.14) nor (b) any fractional Shares or fractional Deposited Securities nor (c) a number of Shares or Deposited Securities which upon application of the ADS to Shares ratio would give rise to fractional ADSs. No Shares shall be accepted for deposit unless accompanied by evidence, if any is required by the Depositary, that is

reasonably satisfactory to the Depositary or the Custodian that all conditions to such deposit have been satisfied by the person depositing such Shares under the laws and regulations of England and Wales and any necessary approval has been granted by any applicable governmental body in England and Wales, if any. The Depositary may issue ADSs against evidence of rights to receive Shares from the Company, any agent of the Company or any custodian, registrar, transfer agent, clearing agency or other entity involved in ownership or transaction records in respect of the Shares. Such evidence of rights shall consist of written blanket or specific guarantees of ownership of Shares furnished by the Company or any such custodian, registrar, transfer agent, clearing agency or other entity involved in ownership or transaction records in respect of the Shares.

Without limitation of the foregoing, the Depositary shall not knowingly accept for deposit under the Deposit Agreement (A) any Shares or other securities required to be registered under the provisions of the Securities Act, unless (i) a registration statement is in effect as to such Shares or other securities or (ii) the deposit is made upon terms contemplated in Section 2.14, or (B) any Shares or other securities the deposit of which would violate any provisions of the Articles of Association of the Company or English law. For purposes of the foregoing sentence, the Depositary shall be entitled to rely upon representations and warranties made or deemed made pursuant to the Deposit Agreement and shall not be required to make any further investigation. The Depositary will comply with written instructions of the Company (received by the Depositary reasonably in advance) not to accept for deposit hereunder any Shares identified in such instructions at such times and under such circumstances as may reasonably be specified in such instructions in order to facilitate the Company's compliance with the securities laws of the United States.

Section 2.4 **Registration and Safekeeping of Deposited Securities.** The Depositary shall instruct the Custodian upon each Delivery of registered Shares being deposited hereunder with the Custodian (or other Deposited Securities pursuant to Article IV hereof), together with the other documents above specified, to present such Shares, together with the appropriate instrument(s) of transfer or endorsement, duly stamped, to the Share Registrar for transfer and registration of the Shares (as soon as transfer and registration can be accomplished and at the expense of the person for whom the deposit is made) in the name of the Depositary, the Custodian or a nominee of either. Deposited Securities shall be held by the Depositary, or by a Custodian for the account and to the order of the Depositary or a nominee of the Depositary, in each case, on behalf of the Holders and Beneficial Owners, at such place(s) as the Depositary or the Custodian shall determine. Notwithstanding anything else contained in the Deposit Agreement, any ADR(s), or any other instruments or agreements relating to the ADSs and the corresponding Deposited Property, the registration of the Deposited Securities in the name of the Depositary, the Custodian or any of their respective nominees, shall, to the maximum extent permitted by applicable law, vest in the Depositary, the Custodian or the applicable nominee the record ownership in the applicable Deposited Securities with the beneficial ownership rights and interests in such Deposited Securities being at all times vested with the Beneficial Owners of the ADSs representing the Deposited Securities. Notwithstanding the foregoing, the Depositary, the Custodian and the applicable nominee shall at all times be entitled to exercise the beneficial ownership rights in all Deposited Property, in each case only on behalf of the Holders and Beneficial Owners of the ADSs representing the Deposited Property, upon the terms set forth in the Deposit Agreement and, if applicable, the ADR(s) representing the ADSs. The Depositary, the Custodian and their respective nominees shall for all purposes be deemed to have all requisite power and authority to act in respect of Deposited Property on behalf of the Holders and Beneficial Owners of ADSs representing the Deposited Property, and upon making payments to, or acting upon instructions from, or information provided by, the Depositary, the Custodian or their respective nominees all persons shall be authorized to rely upon such power and authority.

Section 2.5 **Issuance of ADSs.** The Depositary has made arrangements with the Custodian for the Custodian to confirm to the Depositary upon receipt of a deposit of Shares (i) that a deposit of Shares has been made pursuant to Section 2.3, (ii) that such Deposited Securities have been recorded in the name of the Depositary, the Custodian or a nominee of either on the shareholders' register maintained by or on behalf of the Company by the Share Registrar on the books of CREST, (iii) that all required documents have been received, and (iv) the person(s) to whom or upon whose order ADSs are deliverable in respect thereof and the number of ADSs to be so delivered. Such notification may be made by letter, cable, telex, SWIFT message or, at the risk and expense of the person making the deposit, by facsimile or other means of electronic transmission. Upon receiving such notice from the Custodian, the Depositary, subject to the terms and conditions of the Deposit Agreement and applicable law, shall issue the ADSs representing the Shares so deposited to or upon the order of the person(s) named in the notice delivered to the Depositary and, if applicable, shall execute and deliver at its Principal Office Receipt(s) registered in the name(s) requested by such person(s) and evidencing the aggregate number of ADSs to which such person(s) are entitled, but, in each case, only upon payment to the Depositary of the charges of the Depositary for accepting a deposit of Shares and issuing ADSs (as set forth in Section 5.9 and Exhibit B hereto) and all taxes and governmental

charges and fees payable in connection with such deposit and the transfer of the Shares and the issuance of the ADS(s). The Depositary shall only issue ADSs in whole numbers and deliver, if applicable, ADR(s) evidencing whole numbers of ADSs.

Section 2.6 Transfer, Combination and Split-up of ADRs.

(a) Transfer. The Registrar shall register the transfer of ADRs (and of the ADSs represented thereby) on the books maintained for such purpose and the Depositary shall (x) cancel such ADRs and execute new ADRs evidencing the same aggregate number of ADSs as those evidenced by the ADRs canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs and (z) Deliver such new ADRs to or upon the order of the person entitled thereto, if each of the following conditions has been satisfied: (i) the ADRs have been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a transfer thereof, (ii) the surrendered ADRs have been properly endorsed or are accompanied by proper instruments of transfer (including signature guarantees in accordance with standard securities industry practice), (iii) the surrendered ADRs have been duly stamped (if required by the laws of the State of New York or of the United States), and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 and Exhibit B hereto) have been paid, *subject, however, in each case*, to the terms and conditions of the applicable ADRs, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.

(b) Combination & Split-Up. The Registrar shall register the split-up or combination of ADRs (and of the ADSs represented thereby) on the books maintained for such purpose and the Depositary shall (x) cancel such ADRs and execute new ADRs for the number of ADSs requested, but in the aggregate not exceeding the number of ADSs evidenced by the ADRs canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs and (z) Deliver such new ADRs to or upon the order of the Holder thereof, if each of the following conditions has been satisfied: (i) the ADRs have been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a split-up or combination thereof, and (ii) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 and Exhibit B hereto) have been paid, *subject, however, in each case*, to the terms and conditions of the applicable ADRs, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.

Section 2.7 Surrender of ADSs and Withdrawal of Deposited Securities. The Holder of ADSs shall be entitled to Delivery (at the Custodian's designated office) of the Deposited Securities at the time represented by the ADSs upon satisfaction of each of the following conditions: (i) the Holder (or a duly-authorized attorney of the Holder) has duly Delivered ADSs to the Depositary at its Principal Office (and if applicable, the ADRs evidencing such ADSs) for the purpose of withdrawal of the Deposited Securities represented thereby, (ii) if applicable and so required by the Depositary, the ADRs Delivered to the Depositary for such purpose have been properly endorsed in blank or are accompanied by proper instruments of transfer in blank (including signature guarantees in accordance with standard securities industry

practice), (iii) if so required by the Depositary, the Holder of the ADSs has executed and delivered to the Depositary a written order directing the Depositary to cause the Deposited Securities being withdrawn to be Delivered to or upon the written order of the person(s) designated in such order, and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 and Exhibit B) have been paid, *subject, however, in each case*, to the terms and conditions of the ADRs evidencing the surrendered ADSs, of the Deposit Agreement, of the Company's Articles of Association and of any applicable laws and the rules of CREST, and to any provisions of or governing the Deposited Securities , in each case as in effect at the time thereof.

Upon satisfaction of each of the conditions specified above, the Depositary (i) shall cancel the ADSs Delivered to it (and, if applicable, the ADR(s) evidencing the ADSs so Delivered), (ii) shall direct the Registrar to record the cancellation of the ADSs so Delivered on the books maintained for such purpose, and (iii) shall direct the Custodian to Deliver, or cause the Delivery of, in each case, without unreasonable delay, the Deposited Securities represented by the ADSs so canceled together with any certificate or other document of title for the Deposited Securities, or evidence of the electronic transfer thereof (if available), as the case may be, to or upon the written order of the person(s) designated in the order delivered to the Depositary for such purpose, *subject however, in each case*, to the terms and conditions of the Deposit Agreement, of the ADRs evidencing the ADSs so canceled, of the Articles of Association of the Company, of any applicable laws and of the rules of CREST, and to the terms and conditions of or governing the Deposited Securities, in each case as in effect at the time thereof.

The Depositary shall not accept for surrender ADSs representing less than one (1) Share. In the case of Delivery to it of ADSs representing a number other than a whole number of Shares, the Depositary shall cause ownership of the appropriate whole number of Shares to be Delivered in accordance with the terms hereof, and shall, at the discretion of the Depositary, either (i) return to the person surrendering such ADSs the number of ADSs representing any remaining fractional Share, or (ii) sell or cause to be sold the fractional Share represented by the ADSs so surrendered and remit the proceeds of such sale (net of (a) applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes required to be withheld) to the person surrendering the ADSs.

Notwithstanding anything else contained in any ADR or the Deposit Agreement, the Depositary may make delivery at the Principal Office of the Depositary of Deposited Property consisting of (i) any cash dividends or cash distributions, or (ii) any proceeds from the sale of any non-cash distributions, which are at the time held by the Depositary in respect of the Deposited Securities represented by the ADSs surrendered for cancellation and withdrawal. At the request, risk and expense of any Holder so surrendering ADSs, and for the account of such Holder, the Depositary shall direct the Custodian to forward (to the extent permitted by law) any Deposited Property (other than Deposited Securities) held by the Custodian in respect of such ADSs to the Depositary for delivery at the Principal Office of the Depositary. Such direction shall be given by letter or, at the request, risk and expense of such Holder, by cable, telex or facsimile transmission.

Section 2.8 Limitations on Execution and Delivery, Transfer, etc. of ADSs; Suspension of Delivery, Transfer, etc.

(a) Additional Requirements. As a condition precedent to the execution and Delivery, the registration of issuance, transfer, split-up, combination or surrender, of any ADS, the delivery of any distribution thereon, or the withdrawal of any Deposited Property, the Depositary or the Custodian may require (i) payment from the depositor of Shares or presenter of ADSs or of an ADR of a sum sufficient to reimburse it for any tax or other governmental charge and any stock transfer or registration fee with respect thereto (including any such tax or charge and fee with respect to Shares being deposited or withdrawn) and payment of any applicable fees and charges of the Depositary as provided in Section 5.9 and Exhibit B, (ii) the production of proof reasonably satisfactory to it as to the identity and genuineness of any signature or any other matter contemplated by Section 3.1, and (iii) compliance with (A) any laws or governmental regulations relating to the execution and Delivery of ADRs or ADSs or to the withdrawal of Deposited Securities and (B) such reasonable regulations as the Depositary and the Company may establish consistent with the provisions of the representative ADR, if applicable, the Deposit Agreement and applicable law.

(b) Additional Limitations. The issuance of ADSs against deposits of Shares generally or against deposits of particular Shares may be suspended, or the deposit of particular Shares may be refused, or the registration of transfer of ADSs in particular instances may be refused, or the registration of transfers of ADSs generally may be suspended, during any period when the transfer books of the Company, the Depositary, a Registrar or the Share Registrar are closed or if any such action is deemed necessary or advisable by the Depositary or the Company, in good faith, at any time or from time to time because of any requirement of law or regulation, any government or governmental body or commission or any securities exchange on which the ADSs or Shares are listed, or under any provision of the Deposit Agreement or the representative ADR(s), if applicable, or under any provision of, or governing, the Deposited Securities, or because of a meeting of shareholders of the Company or for any other reason, subject, in all cases, to Section 7.8(a).

(c) Regulatory Restrictions. Notwithstanding any provision of the Deposit Agreement or any ADR(s) to the contrary, Holders are entitled to surrender outstanding ADSs to withdraw the Deposited Securities associated herewith at any time subject only to (i) temporary delays caused by closing the transfer books of the Depositary or the Company or the deposit of Shares in connection with voting at a shareholders' meeting or the payment of dividends, (ii) the payment of fees, taxes and similar charges, (iii) compliance with any U.S. or foreign laws or governmental regulations relating to the ADSs or to the withdrawal of the Deposited Securities, and (iv) other circumstances specifically contemplated by Instruction I.A.(l) of the General Instructions to Form F-6 (as such General Instructions may be amended from time to time).

Section 2.9 Lost ADRs, etc. In case any ADR shall be mutilated, destroyed, lost, or stolen, the Depositary shall execute and deliver a new ADR of like tenor at the expense of the Holder (a) *in the case of a mutilated ADR,* in exchange of and substitution for such mutilated ADR upon cancellation thereof, or (b) *in the case of a destroyed, lost or stolen ADR,* in lieu of and in substitution for such destroyed, lost, or stolen ADR, after the Holder thereof (i) has

submitted to the Depositary a written request for such exchange and substitution before the Depositary has notice that the ADR has been acquired by a bona fide purchaser, (ii) has provided such security or indemnity (including an indemnity bond) as may be required by the Depositary to save it and any of its agents harmless, and (iii) has satisfied any other reasonable requirements imposed by the Depositary, including, without limitation, evidence satisfactory to the Depositary of such destruction, loss or theft of such ADR, the authenticity thereof and the Holder's ownership thereof.

Section 2.10 **Cancellation and Destruction of Surrendered ADRs; Maintenance of Records.** All ADRs surrendered to the Depositary shall be canceled by the Depositary. Canceled ADRs shall not be entitled to any benefits under the Deposit Agreement or be valid or enforceable against the Depositary for any purpose. The Depositary is authorized to destroy ADRs so canceled, provided the Depositary maintains a record of all destroyed ADRs. Any ADSs held in book-entry form (*e.g.*, through accounts at DTC) shall be deemed canceled when the Depositary causes the number of ADSs evidenced by the Balance Certificate to be reduced by the number of ADSs surrendered (without the need to physically destroy the Balance Certificate).

Section 2.11 **Escheatment.** In the event any unclaimed property relating to the ADSs, for any reason, is in the possession of Depositary and has not been claimed by the Holder thereof or cannot be delivered to the Holder thereof through usual channels, the Depositary shall, upon expiration of any applicable statutory period relating to abandoned property laws, escheat such unclaimed property to the relevant authorities in accordance with the laws of each of the relevant States of the United States.

Section 2.12 **Partial Entitlement ADSs.** In the event any Shares are deposited which (i) entitle the holders thereof to receive a per-share distribution or other entitlement in an amount different from the Shares then on deposit or (ii) are not fully fungible (including, without limitation, as to settlement or trading) with the Shares then on deposit (the Shares then on deposit collectively, "Full Entitlement Shares" and the Shares with different entitlement, "Partial Entitlement Shares"), the Depositary shall (i) cause the Custodian to hold Partial Entitlement Shares separate and distinct from Full Entitlement Shares, and (ii) subject to the terms of the Deposit Agreement, issue ADSs representing Partial Entitlement Shares which are separate and distinct from the ADSs representing Full Entitlement Shares, by means of separate CUSIP numbering and legending (if necessary) and, if applicable, by issuing ADRs evidencing such ADSs with applicable notations thereon ("Partial Entitlement ADSs/ADRs" and "Full Entitlement ADSs/ADRs", respectively). If and when Partial Entitlement Shares become Full Entitlement Shares, the Depositary shall (a) give notice thereof to Holders of Partial Entitlement ADSs and give Holders of Partial Entitlement ADRs the opportunity to exchange such Partial Entitlement ADRs for Full Entitlement ADRs, (b) cause the Custodian to transfer the Partial Entitlement Shares into the account of the Full Entitlement Shares, and (c) take such actions as are necessary to remove the distinctions between (i) the Partial Entitlement ADRs and ADSs, on the one hand, and (ii) the Full Entitlement ADRs and ADSs on the other. Holders and Beneficial Owners of Partial Entitlement ADSs shall only be entitled to the entitlements of Partial Entitlement Shares. Holders and Beneficial Owners of Full Entitlement ADSs shall be entitled only to the entitlements of Full Entitlement Shares. All provisions and conditions of the Deposit

Agreement shall apply to Partial Entitlement ADRs and ADSs to the same extent as Full Entitlement ADRs and ADSs, except as contemplated by this Section 2.12. The Depositary is authorized to take any and all other actions as may be necessary (including, without limitation, making the necessary notations on ADRs) to give effect to the terms of this Section 2.12. The Company agrees to give timely written notice to the Depositary if any Shares issued or to be issued are Partial Entitlement Shares and shall assist the Depositary with the establishment of procedures enabling the identification of Partial Entitlement Shares upon Delivery to the Custodian.

Section 2.13 Certificated/Uncertificated ADSs. Notwithstanding any other provision of the Deposit Agreement, the Depositary may, at any time and from time to time, issue ADSs that are not evidenced by ADRs (such ADSs, the "Uncertificated ADS(s)" and the ADS(s) evidenced by ADR(s), the "Certificated ADS(s)"). When issuing and maintaining Uncertificated ADS(s) under the Deposit Agreement, the Depositary shall at all times be subject to (i) the standards applicable to registrars and transfer agents maintaining direct registration systems for equity securities in New York and issuing uncertificated securities under New York law, and (ii) the terms of New York law applicable to uncertificated equity securities. Uncertificated ADSs shall not be represented by any instruments but shall be evidenced by registration in the books of the Depositary maintained for such purpose. Holders of Uncertificated ADSs, that are not subject to any registered pledges, liens, restrictions or adverse claims of which the Depositary has notice at such time, shall at all times have the right to exchange the Uncertificated ADS(s) for Certificated ADS(s) of the same type and class, subject in each case to (x) the applicable laws and any rules and regulations the Depositary may have established in respect of the Uncertificated ADSs, and (y) the continued availability of Certificated ADSs in the U.S. Holders of Certificated ADSs shall, if the Depositary maintains a direct registration system for the ADSs, have the right to exchange the Certificated ADSs for Uncertificated ADSs upon (i) the due surrender of the Certificated ADS(s) to the Depositary for such purpose and (ii) the presentation of a written request to that effect to the Depositary, subject in each case to (a) all liens and restrictions noted on the ADR evidencing the Certificated ADS(s) and all adverse claims of which the Depositary then has notice, (b) the terms of the Deposit Agreement and the rules and regulations that the Depositary may establish for such purposes hereunder, (c) applicable law, and (d) payment of the Depositary fees and expenses applicable to such exchange of Certificated ADS(s) for Uncertificated ADS(s). Uncertificated ADSs shall in all material respects be identical to Certificated ADS(s) of the same type and class, except that (i) no ADR(s) shall be, or shall need to be, issued to evidence Uncertificated ADS(s), (ii) Uncertificated ADS(s) shall, subject to the terms of the Deposit Agreement, be transferable upon the same terms and conditions as uncertificated securities under New York law, (iii) the ownership of Uncertificated ADS(s) shall be recorded on the books of the Depositary maintained for such purpose and evidence of such ownership shall be reflected in periodic statements provided by the Depositary to the Holder(s) in accordance with applicable New York law, (iv) the Depositary may from time to time, upon notice to the Holders of Uncertificated ADSs affected thereby, establish rules and regulations, and amend or supplement existing rules and regulations, as may be deemed reasonably necessary to maintain Uncertificated ADS(s) on behalf of Holders, provided that (a) such rules and regulations do not conflict with the terms of the Deposit Agreement and applicable law, and (b) the terms of such rules and regulations are

readily available to Holders upon request, (v) the Uncertificated ADS(s) shall not be entitled to any benefits under the Deposit Agreement or be valid or enforceable for any purpose against the Depositary or the Company unless such Uncertificated ADS(s) is/are registered on the books of the Depositary maintained for such purpose, (vi) the Depositary may, in connection with any deposit of Shares resulting in the issuance of Uncertificated ADSs and with any transfer, pledge, release and cancellation of Uncertificated ADSs, require the prior receipt of such documentation as the Depositary may deem reasonably appropriate, and (vii) upon termination of the Deposit Agreement, the Depositary shall not require Holders of Uncertificated ADSs to affirmatively instruct the Depositary before remitting proceeds from the sale of the Deposited Property represented by such Holders' Uncertificated ADSs under the terms of Section 6.2. When issuing ADSs under the terms of the Deposit Agreement, including, without limitation, issuances pursuant to Sections 2.5, 4.2, 4.3, 4.4, 4.5 and 4.11, the Depositary may in its discretion determine to issue Uncertificated ADSs rather than Certificated ADSs, unless otherwise specifically instructed by the applicable Holder to issue Certificated ADSs. All provisions and conditions of the Deposit Agreement shall apply to Uncertificated ADSs to the same extent as to Certificated ADSs, except as contemplated by this Section 2.13. The Depositary is authorized and directed to take any and all actions and establish any and all procedures deemed reasonably necessary to give effect to the terms of this Section 2.13. Any references in the Deposit Agreement or any ADR(s) to the terms "American Depositary Share(s)" or "ADS(s)" shall, unless the context otherwise requires, include Certificated ADS(s) and Uncertificated ADS(s). Except as set forth in this Section 2.13 and except as required by applicable law, the Uncertificated ADSs shall be treated as ADSs issued and outstanding under the terms of the Deposit Agreement. In the event that, in determining the rights and obligations of parties hereto with respect to any Uncertificated ADSs, any conflict arises between (a) the terms of the Deposit Agreement (other than this Section 2.13) and (b) the terms of this Section 2.13, the terms and conditions set forth in this Section 2.13 shall be controlling and shall govern the rights and obligations of the parties to the Deposit Agreement pertaining to the Uncertificated ADSs.

Section 2.14 **Restricted ADSs.** The Depositary shall, at the request and expense of the Company, establish procedures enabling the deposit hereunder of Shares that are Restricted Securities in order to enable the holder of such Shares to hold its ownership interests in such Restricted Securities in the form of ADSs issued under the terms hereof (such Shares, "Restricted Shares"). Upon receipt of a written request from the Company to accept Restricted Shares for deposit hereunder, the Depositary agrees to establish procedures permitting the deposit of such Restricted Shares and the issuance of ADSs representing the right to receive, subject to the terms of the Deposit Agreement and the applicable ADR (if issued as a Certificated ADS), such deposited Restricted Shares (such ADSs, the "Restricted ADSs," and the ADRs evidencing such Restricted ADSs, the "Restricted ADRs"). Notwithstanding anything contained in this Section 2.14, the Depositary and the Company may, to the extent not prohibited by law, agree to issue the Restricted ADSs in uncertificated form ("Uncertificated Restricted ADSs") upon such terms and conditions as the Company and the Depositary may deem necessary and appropriate. The Company shall assist the Depositary in the establishment of such procedures and agrees that it shall take all steps necessary and satisfactory to the Depositary to ensure that the establishment of such procedures does not violate the provisions of the Securities Act or any other applicable laws. The depositors of such Restricted Shares and the Holders of the Restricted

ADSs may be required prior to the deposit of such Restricted Shares, the transfer of the Restricted ADRs and Restricted ADSs or the withdrawal of the Restricted Shares represented by Restricted ADSs to provide such written certifications or agreements as the Depositary or the Company may require. The Company shall provide to the Depositary in writing the legend(s) to be affixed to the Restricted ADRs (if the Restricted ADSs are to be issued as Certificated ADSs**)**, or to be included in the statements issued from time to time to Holders of Uncertificated ADSs (if issued as Uncertificated Restricted ADSs), which legends shall (i) be in a form reasonably satisfactory to the Depositary and (ii) contain the specific circumstances under which the Restricted ADSs, and, if applicable, the Restricted ADRs evidencing the Restricted ADSs, may be transferred or the Restricted Shares withdrawn. The Restricted ADSs issued upon the deposit of Restricted Shares shall be separately identified on the books of the Depositary and the Restricted Shares so deposited shall, to the extent required by law, be held separate and distinct from the other Deposited Securities held hereunder. The Restricted ADSs shall not be eligible for inclusion in any book-entry settlement system, including, without limitation, DTC, and shall not in any way be fungible with the ADSs issued under the terms hereof that are not Restricted ADSs. The Restricted ADSs, and, if applicable, the Restricted ADRs evidencing the Restricted ADSs, shall be transferable only by the Holder thereof upon delivery to the Depositary of (i) all documentation otherwise contemplated by the Deposit Agreement and (ii) an opinion of counsel satisfactory to the Depositary setting forth, *inter alia*, the conditions upon which the Restricted ADSs presented, and, if applicable, the Restricted ADRs evidencing the Restricted ADSs, are transferable by the Holder thereof under applicable securities laws and the transfer restrictions contained in the legend applicable to the Restricted ADSs presented for transfer. Except as set forth in this Section 2.14 and except as required by applicable law, the Restricted ADSs and the Restricted ADRs evidencing Restricted ADSs shall be treated as ADSs and ADRs issued and outstanding under the terms of the Deposit Agreement. In the event that, in determining the rights and obligations of parties hereto with respect to any Restricted ADSs, any conflict arises between (a) the terms of the Deposit Agreement (other than this Section 2.14) and (b) the terms of (i) this Section 2.14 or (ii) the applicable Restricted ADR, the terms and conditions set forth in this Section 2.14 and of the Restricted ADR shall be controlling and shall govern the rights and obligations of the parties to the Deposit Agreement pertaining to the deposited Restricted Shares, the Restricted ADSs and Restricted ADRs.

If the Restricted ADRs, the Restricted ADSs and the Restricted Shares cease to be Restricted Securities, the Depositary, upon receipt of (x) an opinion of counsel satisfactory to the Depositary setting forth, *inter alia*, that the Restricted ADRs, the Restricted ADSs and the Restricted Shares are not as of such time Restricted Securities, and (y) instructions from the Company to remove the restrictions applicable to the Restricted ADRs, the Restricted ADSs and the Restricted Shares, shall (i) eliminate the distinctions and separations that may have been established between the applicable Restricted Shares held on deposit under this Section 2.14 and the other Shares held on deposit under the terms of the Deposit Agreement that are not Restricted Shares, (ii) treat the newly unrestricted ADRs and ADSs on the same terms as, and fully fungible with, the other ADRs and ADSs issued and outstanding under the terms of the Deposit Agreement that are not Restricted ADRs or Restricted ADSs, and (iii) take all actions necessary to remove any distinctions, limitations and restrictions previously existing under this Section 2.14 between the applicable Restricted ADRs and Restricted ADSs, respectively, on the one

hand, and the other ADRs and ADSs that are not Restricted ADRs or Restricted ADSs, respectively, on the other hand, including, without limitation, by making the newly-unrestricted ADSs eligible for inclusion in the applicable book-entry settlement systems.

ARTICLE III

CERTAIN OBLIGATIONS OF HOLDERS AND BENEFICIAL OWNERS OF ADSs

Section 3.1 **Proofs, Certificates and Other Information.** Any person presenting Shares for deposit, any Holder and any Beneficial Owner may be required, and every Holder and Beneficial Owner agrees, from time to time to provide to the Depositary and the Custodian such proof of citizenship or residence, taxpayer status, payment of all applicable taxes or other governmental charges, exchange control approval, legal or beneficial ownership of ADSs and Deposited Property, compliance with applicable laws, the terms of the Deposit Agreement or the ADR(s) evidencing the ADSs and the provisions of, or governing, the Deposited Property, to execute such certifications and to make such representations and warranties, and to provide such other information and documentation (or, in the case of Shares in registered form presented for deposit, such information relating to the registration on the books of the Company or of the Share Registrar) as the Depositary or the Custodian may deem necessary or proper or as the Company may reasonably require by written request to the Depositary consistent with its obligations under the Deposit Agreement and the applicable ADR(s). The Depositary and the Registrar, as applicable, may and at the reasonable request of the Company, shall, to the extent practicable and subject to applicable law, withhold the execution or delivery or registration of transfer of any ADR or ADS or the distribution or sale of any dividend or distribution of rights or of the proceeds thereof or, to the extent not limited by the terms of Section 7.8(a), the delivery of any Deposited Property until such proof or other information is filed or such certifications are executed, or such representations and warranties are made, or such other documentation or information provided, in each case to the Depositary's, the Registrar's and the Company's satisfaction. The Depositary shall provide the Company, in a timely manner, with copies or originals if necessary and appropriate of (i) any such proofs of citizenship or residence, taxpayer status, or exchange control approval or copies of written representations and warranties which it receives from Holders and Beneficial Owners, and (ii) any other information or documents which the Company may reasonably request and which the Depositary shall request and receive from any Holder or Beneficial Owner or any person presenting Shares for deposit or ADSs for cancellation, transfer or withdrawal. Nothing herein shall obligate the Depositary to (i) obtain any information for the Company if not provided by the Holders or Beneficial Owners, or (ii) verify or vouch for the accuracy of the information so provided by the Holders or Beneficial Owners.

Section 3.2 **Liability for Taxes and Other Charges.** Any tax or other governmental charge payable by the Custodian or by the Depositary with respect to any Deposited Property, ADSs or ADRs shall be payable by the Holders and Beneficial Owners to the Depositary. The Company, the Custodian and/or the Depositary may withhold or deduct from any distributions made in respect of Deposited Property, and may sell for the account of a Holder and/or Beneficial Owner any or all of the Deposited Property and apply such distributions and sale

proceeds in payment of, any taxes (including applicable interest and penalties) or charges that are or may be payable by Holders or Beneficial Owners in respect of the ADSs, Deposited Property and ADRs, the Holder and the Beneficial Owner remaining liable for any deficiency. The Custodian may refuse the deposit of Shares and the Depositary may refuse to issue ADSs, to deliver ADRs, register the transfer of ADSs, register the split-up or combination of ADRs and (subject to Section 7.8(a)) the withdrawal of Deposited Property until payment in full of such tax, charge, penalty or interest is received. Every Holder and Beneficial Owner agrees to indemnify the Depositary, the Company, the Custodian, and any of their agents, officers, employees and Affiliates for, and to hold each of them harmless from, any claims with respect to taxes (including applicable interest and penalties thereon) arising from any tax benefit obtained for such Holder and/or Beneficial Owner. The obligations of Holders and Beneficial Owners under this Section 3.2 shall survive any transfer of ADSs, any cancellation of ADSs and withdrawal of Deposited Securities, and the termination of the Deposit Agreement.

Section 3.3 **Representations and Warranties on Deposit of Shares.** Each person depositing Shares under the Deposit Agreement shall be deemed thereby to represent and warrant that (i) such Shares and the certificates therefor are duly authorized, validly allotted and issued, fully paid, not subject to any call for the payment of further capital and legally obtained by such person, (ii) all preemptive (and similar) rights, if any, with respect to such Shares have been validly waived, disapplied or exercised, (iii) the person making such deposit is duly authorized so to do, (iv) the Shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, (v) the Shares presented for deposit are not, and the ADSs issuable upon such deposit will not be, Restricted Securities (except as contemplated in Section 2.14), (vi) the Shares presented for deposit have not been stripped of any rights or entitlements and (vii) the deposit of the Shares does not violate any applicable provisions of English law. Such representations and warranties shall survive the deposit and withdrawal of Shares, the issuance and cancellation of ADSs in respect thereof and the transfer of such ADSs. If any such representations or warranties are false in any way, the Company and the Depositary shall be authorized, at the cost and expense of the person depositing Shares, to take any and all actions necessary to correct the consequences thereof.

Section 3.4 **Compliance with Information Requests.** Notwithstanding any other provision of the Deposit Agreement or any ADR(s), each Holder and Beneficial Owner agrees to comply with requests from the Company pursuant to applicable law, the rules and requirements of any stock exchange on which the Shares or ADSs are, or will be, registered, traded or listed or the Articles of Association of the Company, which are made to provide information, *inter alia*, as to the capacity in which such Holder or Beneficial Owner owns ADSs (and Shares as the case may be) and regarding the identity of any other person(s) interested in such ADSs and the nature of such interest and various other matters, whether or not they are Holders and/or Beneficial Owners at the time of such request. The Depositary agrees to use its reasonable efforts to forward, upon the request of the Company and at the Company's expense, any such request from the Company to the Holders and to forward to the Company, as promptly as practicable, any such responses to such requests received by the Depositary.

Section 3.5 **Ownership Restrictions.** Notwithstanding any other provision in the Deposit Agreement or any ADR, the Company may restrict transfers of the Shares where such

transfer might result in ownership of Shares exceeding limits imposed by applicable law or the Articles of Association of the Company. The Company may also restrict, in such manner as it deems appropriate, transfers of the ADSs where such transfer may result in the total number of Shares represented by the ADSs owned by a single Holder or Beneficial Owner to exceed any such limits. The Company may, in its sole discretion but subject to applicable law, instruct the Depositary to take action with respect to the ownership interest of any Holder or Beneficial Owner in excess of the limits set forth in the preceding sentence, including, but not limited to, the imposition of restrictions on the transfer of ADSs, the removal or limitation of voting rights or mandatory sale or disposition on behalf of a Holder or Beneficial Owner of the Shares represented by the ADSs held by such Holder or Beneficial Owner in excess of such limitations, if and to the extent such disposition is permitted by applicable law and the Articles of Association of the Company. Nothing herein shall be interpreted as obligating the Depositary or the Company to ensure compliance with the ownership restrictions described in this Section 3.5.

Notwithstanding any provision of the Deposit Agreement or of the ADRs and without limiting the foregoing, by being a Holder of an ADR, each such Holder agrees to provide such information as the Company may request in a disclosure notice (a "Disclosure Notice") given pursuant to the U.K. Companies Act 2006 (as amended from time to time and including any statutory modification or re-enactment thereof, the "Companies Act") or the Articles of Association of the Company. By accepting or holding an ADR, each Holder acknowledges that it understands that failure to comply with a Disclosure Notice may result in the imposition of sanctions against the holder of the Shares in respect of which the non-complying person is or was, or appears to be or has been, interested as provided in the Companies Act and the Articles of Association which currently include, the withdrawal of the voting rights of such Shares and the imposition of restrictions on the rights to receive dividends on and to transfer such Shares.

The Company reserves the right to instruct Holders to deliver their ADSs for cancellation and withdrawal of the Deposited Securities so as to permit the Company to deal directly with the Holder thereof as a holder of Shares and Holders agree to comply with such instructions. The Depositary agrees to cooperate with the Company in its efforts to inform Holders of the Company's exercise of its rights under this paragraph and agrees to consult with, and provide reasonable assistance without risk, liability or expense on the part of the Depositary, to the Company on the manner or manners in which it may enforce such rights with respect to any Holder.

Section 3.6 **Reporting Obligations and Regulatory Approvals.** Applicable laws and regulations may require holders and beneficial owners of Shares, including the Holders and Beneficial Owners of ADSs, to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. Holders and Beneficial Owners of ADSs are solely responsible for determining and complying with such reporting requirements and obtaining such approvals. Each Holder and each Beneficial Owner hereby agrees to make such determination, file such reports, and obtain such approvals to the extent and in the form required by applicable laws and regulations as in effect from time to time. Neither the Depositary, the Custodian, the Company or any of their respective agents or affiliates shall be required to take any actions whatsoever on behalf of Holders or Beneficial Owners to determine or satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

ARTICLE IV

THE DEPOSITED SECURITIES

Section 4.1 **Cash Distributions.** Whenever the Company intends to make a distribution of a cash dividend or other cash distribution in respect of any Deposited Securities, the Company shall give notice thereof to the Depositary at least twenty (20) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable for determining the holders of Deposited Securities entitled to receive such distribution. Upon the timely receipt of such notice, the Depositary shall establish an ADS Record Date upon the terms described in Section 4.9. Upon receipt of confirmation of the receipt of (x) any cash dividend or other cash distribution on any Deposited Securities, or (y) proceeds from the sale of any Deposited Property held in respect of the ADSs under the terms hereof, the Depositary will (i) if at the time of receipt thereof any amounts received in a Foreign Currency can, in the judgment of the Depositary (pursuant to Section 4.8), be converted on a practicable basis into Dollars transferable to the United States, promptly convert or cause to be converted such cash dividend, distribution or proceeds into Dollars (on the terms described in Section 4.8), (ii) if applicable and unless previously established, establish the ADS Record Date upon the terms described in Section 4.9, and (iii) distribute promptly the amount thus received (net of (a) the applicable fees and charges set forth in the Fee Schedule attached hereto as Exhibit B, and (b) applicable taxes required to be withheld in connection with the distribution) to the Holders entitled thereto as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date. The Depositary shall distribute only such amount, however, as can be distributed without attributing to any Holder a fraction of one cent, and any balance not so distributed shall be held by the Depositary (without liability for interest thereon) and shall be added to and become part of the next sum received by the Depositary for distribution to Holders of ADSs outstanding at the time of the next distribution. If the Company, the Custodian or the Depositary is required to withhold and does withhold from any cash dividend or other cash distribution in respect of any Deposited Securities, or from any cash proceeds from the sales of Deposited Property, an amount on account of taxes, duties or other governmental charges, the amount distributed to Holders on the ADSs shall be reduced accordingly. Such withheld amounts shall be forwarded by the Company, the Custodian or the Depositary to the relevant governmental authority. Evidence of payment thereof by the Company shall be forwarded by the Company to the Depositary upon request. The Depositary will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable Holders and Beneficial Owners of ADSs until the distribution can be effected or the funds that the Depositary holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in this Section 4.1, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.1, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.1 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

Section 4.2 **Distribution in Shares.** Whenever the Company intends to make a distribution that consists of a dividend in, or free distribution of, Shares, the Company shall give timely notice thereof to the Depositary at least twenty(20) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution, specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such distribution. Upon the timely receipt of such notice from the Company, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9. Upon receipt of confirmation from the Custodian of the receipt of the Shares so distributed by the Company, the Depositary shall either (i) subject to Section 5.9, distribute to the Holders as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date, additional ADSs, which represent in the aggregate the number of Shares received as such dividend, or free distribution, subject to the other terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes to be withheld), or (ii) if additional ADSs are not so distributed, take all actions necessary so that each ADS issued and outstanding after the ADS Record Date shall, to the extent permissible by law, thenceforth also represent rights and interests in the additional integral number of Shares distributed upon the Deposited Securities represented thereby (net of (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes). In lieu of delivering fractional ADSs, the Depositary shall sell the number of Shares or ADSs, as the case may be, represented by the aggregate of such fractions and distribute the net proceeds upon the terms described in Section 4.1. In the event that the Depositary determines that any distribution in property (including Shares) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, or, if the Company in the fulfillment of its obligation under Section 5.7, has furnished an opinion of U.S. counsel determining that Shares must be registered under the Securities Act or other laws in order to be distributed to Holders (and no such registration statement has been declared effective), the Depositary may dispose of all or a portion of such property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable, and the Depositary shall distribute the net proceeds of any such sale (after deduction of (a) applicable taxes required to be withheld and (b) fees and charges of, and expenses incurred by, the Depositary) to Holders entitled thereto upon the terms described in Section 4.1. The Depositary shall hold and/or distribute any unsold balance of such property in accordance with the provisions of the Deposit Agreement. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in this Section 4.2, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.2, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.2 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

Section 4.3 **Elective Distributions in Cash or Shares.** Whenever the Company intends to make a distribution payable at the election of the holders of Deposited Securities in cash or in additional Shares, the Company shall give timely notice thereof to the Depositary at least forty-five (45) days (or such other number of days as mutually agreed to in writing by the

Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such elective distribution and whether or not it wishes such elective distribution to be made available to Holders of ADSs. Upon the timely receipt of a notice indicating that the Company wishes such elective distribution to be made available to Holders of ADSs, the Depositary shall consult with the Company to determine, and the Company shall assist the Depositary in its determination, whether it is lawful and reasonably practicable to make such elective distribution available to the Holders of ADSs. The Depositary shall make such elective distribution available to Holders only if (i) the Company shall have timely requested that the elective distribution be made available to Holders, (ii) the Depositary shall have determined that such distribution is reasonably practicable and (iii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7. If the above conditions are not satisfied or if the Company requests such elective distribution not to be made available to Holders of ADSs, the Depositary shall establish the ADS Record Date on the terms described in Section 4.9 and, to the extent permitted by law, distribute to the Holders, on the basis of the same determination as is made in England and Wales in respect of the Shares for which no election is made, either (X) cash upon the terms described in Section 4.1 or (Y) additional ADSs representing such additional Shares upon the terms described in Section 4.2. If the above conditions are satisfied, the Depositary shall establish an ADS Record Date on the terms described in Section 4.9 and establish procedures to enable Holders to elect the receipt of the proposed distribution in cash or in additional ADSs. The Company shall assist the Depositary in establishing such procedures to the extent necessary. If a Holder elects to receive the proposed distribution (X) in cash, the distribution shall be made upon the terms described in Section 4.1, or (Y) in ADSs, the distribution shall be made upon the terms described in Section 4.2. Nothing herein shall obligate the Depositary to make available to Holders a method to receive the elective distribution in Shares (rather than ADSs). There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive elective distributions on the same terms and conditions as the holders of Shares. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for in this Section 4.3, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.3, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.3 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

Section 4.4 Distribution of Rights to Purchase Additional ADSs.

(a) Distribution to ADS Holders. Whenever the Company intends to distribute to the holders of the Deposited Securities rights to subscribe for additional Shares, the Company shall give timely notice thereof to the Depositary at least forty-five (45) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the proposed distribution specifying, *inter alia*, the record date applicable to holders of Deposited Securities entitled to receive such distribution and whether or not it wishes such rights to be made available to Holders of ADSs. Upon the timely receipt of a notice indicating that the Company wishes such rights to be made available to Holders of ADSs, the Depositary shall consult with the Company to determine, and the Company shall assist the Depositary in its

determination, whether it is lawful and reasonably practicable to make such rights available to the Holders. The Depositary shall make such rights available to Holders only if (i) the Company shall have timely requested that such rights be made available to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7, and (iii) the Depositary shall have determined that such distribution of rights is reasonably practicable. In the event any of the conditions set forth above are not satisfied or if the Company requests that the rights not be made available to Holders of ADSs, the Depositary shall proceed with the sale of the rights as contemplated in Section 4.4(b) below. In the event all conditions set forth above are satisfied, the Depositary shall establish the ADS Record Date (upon the terms described in Section 4.9) and establish procedures to (x) distribute rights to purchase additional ADSs (by means of warrants or otherwise), (y) enable the Holders to exercise such rights (upon payment of the subscription price and of the applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes), and (z) deliver ADSs upon the valid exercise of such rights. The Company shall assist the Depositary to the extent necessary in establishing such procedures. Nothing herein shall obligate the Depositary to make available to the Holders a method to exercise rights to subscribe for Shares (rather than ADSs).

(b) **Sale of Rights.** If (i) the Company does not timely request the Depositary to make the rights available to Holders or requests that the rights not be made available to Holders, (ii) the Depositary fails to receive satisfactory documentation within the terms of Section 5.7, or determines it is not reasonably practicable to make the rights available to Holders, or (iii) any rights made available are not exercised and appear to be about to lapse, the Depositary shall determine whether it is lawful and reasonably practicable to sell such rights, in a riskless principal capacity, at such place and upon such terms (including public or private sale) as it may deem practicable. The Company shall assist the Depositary to the extent necessary to determine such legality and practicability. The Depositary shall, upon such sale, convert and distribute proceeds of such sale (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) upon the terms set forth in Section 4.1.

(c) **Lapse of Rights.** If the Depositary is unable to make any rights available to Holders upon the terms described in Section 4.4(a) or to arrange for the sale of the rights upon the terms described in Section 4.4(b), the Depositary shall allow such rights to lapse.

The Depositary shall not be liable for (i) any failure to accurately determine whether it may be lawful or practicable to make such rights available to Holders in general or any Holders in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or exercise, or (iii) the content of any materials forwarded to the Holders on behalf of the Company in connection with the rights distribution.

Notwithstanding anything to the contrary in this Section 4.4, if registration (under the Securities Act or any other applicable law) of the rights or the securities to which any rights relate may be required in order for the Company to offer such rights or such securities to Holders and to sell the securities represented by such rights, the Depositary will not distribute such rights to the Holders (i) unless and until a registration statement under the Securities Act (or other applicable law) covering such offering is in effect or (ii) unless the Company furnishes the Depositary opinion(s) of counsel for the Company in the United States and counsel to the

Company in any other applicable country in which rights would be distributed, in each case satisfactory to the Depositary, to the effect that the offering and sale of such securities to Holders and Beneficial Owners are exempt from, or do not require registration under, the provisions of the Securities Act or any other applicable laws.

In the event that the Company, the Depositary or the Custodian shall be required to withhold and does withhold from any distribution of Deposited Property (including rights) an amount on account of taxes or other governmental charges, the amount distributed to the Holders of ADSs shall be reduced accordingly. In the event that the Depositary determines that any distribution of Deposited Property (including Shares and rights to subscribe therefor) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, the Depositary may dispose of all or a portion of such Deposited Property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable to pay any such taxes or charges.

There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive or exercise rights on the same terms and conditions as the holders of Shares or be able to exercise such rights. Nothing herein shall obligate the Company to file any registration statement in respect of any rights or Shares or other securities to be acquired upon the exercise of such rights.

Section 4.5 Distributions Other Than Cash, Shares or Rights to Purchase Shares.

(a) Whenever the Company intends to distribute to the holders of Deposited Securities property other than cash, Shares or rights to purchase additional Shares, the Company shall give timely notice thereof to the Depositary and shall indicate whether or not it wishes such distribution to be made to Holders of ADSs. Upon receipt of a notice indicating that the Company wishes such distribution to be made to Holders of ADSs, the Depositary shall consult with the Company, and the Company shall assist the Depositary, to determine whether such distribution to Holders is lawful and reasonably practicable. The Depositary shall not make such distribution unless (i) the Company shall have requested the Depositary to make such distribution to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7, and (iii) the Depositary shall have determined that such distribution is reasonably practicable.

(b) Upon receipt of satisfactory documentation and the request of the Company to distribute property to Holders of ADSs and after making the requisite determinations set forth in (a) above, the Depositary shall distribute the property so received to the Holders of record, as of the ADS Record Date, in proportion to the number of ADSs held by them respectively and in such manner as the Depositary may deem practicable for accomplishing such distribution (i) upon receipt of payment or net of the applicable fees and charges of, and expenses incurred by, the Depositary, and (ii) net of any applicable taxes required to be withheld. The Depositary may dispose of all or a portion of the property so distributed and deposited, in such amounts and in such manner (including public or private sale) as the Depositary may deem practicable or necessary to satisfy any taxes (including applicable interest and penalties) or other governmental charges applicable to the distribution.

(c) If (i) the Company does not request the Depositary to make such distribution to Holders or requests the Depositary not to make such distribution to Holders, (ii) the Depositary does not receive satisfactory documentation within the terms of Section 5.7, or (iii) the Depositary determines that all or a portion of such distribution is not reasonably practicable, the Depositary shall sell or cause such property to be sold in a public or private sale, at such place or places and upon such terms as it may deem practicable and shall (i) cause the proceeds of such sale, if any, to be converted into Dollars and (ii) distribute the proceeds of such conversion received by the Depositary (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) to the Holders as of the ADS Record Date upon the terms of Section 4.1. If the Depositary is unable to sell such property, the Depositary may dispose of such property for the account of the Holders in any way it deems reasonably practicable under the circumstances.

(d) Neither the Depositary nor the Company shall be liable for (i) any failure to accurately determine whether it is lawful or practicable to make the property described in this Section 4.5 available to Holders in general or any Holders in particular, nor (ii) any loss incurred in connection with the sale or disposal of such property.

Section 4.6 **Distributions with Respect to Deposited Securities in Bearer Form.** Subject to the terms of this Article IV, distributions in respect of Deposited Securities that are held by the Depositary or the Custodian in bearer form shall be made to the Depositary for the account of the respective Holders of ADS(s) with respect to which any such distribution is made upon due presentation by the Depositary or the Custodian to the Company of any relevant coupons, talons, or certificates. The Company shall promptly notify the Depositary of such distributions. The Depositary or the Custodian shall promptly present such coupons, talons or certificates, as the case may be, in connection with any such distribution.

Section 4.7 **Redemption.** If the Company intends to exercise any right of redemption in respect of any of the Deposited Securities, the Company shall give notice thereof to the Depositary at least forty-five (45) days (or such other number of days as mutually agreed to in writing by the Depositary and the Company) prior to the intended date of redemption which notice shall set forth the particulars of the proposed redemption. Upon timely receipt of (i) such notice and (ii) satisfactory documentation given by the Company to the Depositary within the terms of Section 5.7, and only if after consultation between the Depositary and the Company, the Depositary shall have determined that such proposed redemption is practicable, the Depositary shall provide to each Holder a notice setting forth the intended exercise by the Company of the redemption rights and any other particulars set forth in the Company's notice to the Depositary. The Depositary shall instruct the Custodian to present to the Company the Deposited Securities in respect of which redemption rights are being exercised against payment of the applicable redemption price. Upon receipt of confirmation from the Custodian that the redemption has taken place and that funds representing the redemption price have been received, the Depositary shall convert, transfer, and distribute the proceeds (net of applicable (a) fees and charges of, and the expenses incurred by, the Depositary, and (b) taxes), retire ADSs and cancel ADRs, if applicable, upon delivery of such ADSs by Holders thereof and the terms set forth in Sections 4.1 and 6.2. If less than all outstanding Deposited Securities are redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as may be determined by the Depositary after

consultation with the Company. The redemption price per ADS shall be the dollar equivalent of the per share amount received by the Depositary (adjusted to reflect the ADS(s)-to-Share(s) ratio) upon the redemption of the Deposited Securities represented by ADSs (subject to the terms of Section 4.8 and the applicable fees and charges of, and expenses incurred by, the Depositary, and applicable taxes) multiplied by the number of Deposited Securities represented by each ADS redeemed.

Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed redemption provided for in this Section 4.7, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in this Section 4.7, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in this Section 4.7 where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

Section 4.8 **Conversion of Foreign Currency.** Whenever the Depositary or the Custodian shall receive Foreign Currency, by way of dividends or other distributions or the net proceeds from the sale of Deposited Property, which in the judgment of the Depositary can at such time be converted on a practicable basis, by sale or in any other manner that it may determine in accordance with applicable law, into Dollars transferable to the United States and distributable to the Holders entitled thereto, the Depositary shall convert or cause to be converted, by sale or in any other manner that it may determine, such Foreign Currency into Dollars, and shall distribute such Dollars (net of the fees and charges set forth in the Fee Schedule attached hereto as Exhibit B, and applicable taxes withheld) in accordance with the terms of the applicable sections of the Deposit Agreement. The Depositary and/or its agent (which may be a division, branch or Affiliate of the Depositary) may act as principal for any conversion of Foreign Currency. If the Depositary shall have distributed warrants or other instruments that entitle the holders thereof to such Dollars, the Depositary shall distribute such Dollars to the holders of such warrants and/or instruments upon surrender thereof for cancellation, in either case without liability for interest thereon. Such distribution may be made upon an averaged or other practicable basis without regard to any distinctions among Holders on account of any application of exchange restrictions or otherwise.

If such conversion or distribution generally or with regard to a particular Holder can be effected only with the approval or license of any government or agency thereof, the Depositary shall have authority to file such application for approval or license, if any, as it may deem desirable. In no event, however, shall the Depositary be obligated to make such a filing.

If at any time the Depositary shall determine that in its judgment the conversion of any Foreign Currency and the transfer and distribution of proceeds of such conversion received by the Depositary is not practicable or lawful, or if any approval or license of any governmental authority or agency thereof that is required for such conversion, transfer and distribution is denied or, in the opinion of the Depositary, not obtainable at a reasonable cost or within a reasonable period, the Depositary may, in its reasonable discretion, (i) make such conversion and distribution in Dollars to the Holders for whom such conversion, transfer and distribution is lawful and practicable, (ii) distribute the Foreign Currency (or an appropriate document

evidencing the right to receive such Foreign Currency) to Holders for whom this is lawful and practicable, or (iii) hold (or cause the Custodian to hold) such Foreign Currency (without liability for interest thereon) for the respective accounts of the Holders entitled to receive the same.

Section 4.9 **Fixing of ADS Record Date.** Whenever (a) the Depositary shall receive notice of the fixing of a record date by the Company for the determination of holders of Deposited Securities entitled to receive any distribution (whether in cash, Shares, rights, or other distribution), (b) for any reason the Depositary causes a change in the number of Shares that are represented by each ADS, (c) the Depositary shall receive notice of any meeting of, or solicitation of consents or proxies of, holders of Shares or other Deposited Securities, or (d) the Depositary shall find it necessary or convenient in connection with the giving of any notice, solicitation of any consent or any other matter, the Depositary shall fix the record date (the "ADS Record Date") for the determination of the Holders of ADS(s) who shall be entitled to receive such distribution, to give instructions for the exercise of voting rights at any such meeting, to give or withhold such consent, to receive such notice or solicitation or to otherwise take action, or to exercise the rights of Holders with respect to such changed number of Shares represented by each ADS. The Depositary shall make reasonable efforts to establish the ADS Record Date as closely as practicable to the applicable record date for the Deposited Securities (if any) set by the Company in England and Wales and shall not announce the establishment of any ADS Record Date prior to the relevant corporate action having been made public by the Company (if such corporate action affects the Deposited Securities). Subject to applicable law and the provisions of Section 4.1 through 4.8 and to the other terms and conditions of the Deposit Agreement, only the Holders of ADSs at the close of business in New York on such ADS Record Date shall be entitled to receive such distribution, to give such voting instructions, to receive such notice or solicitation, or otherwise take action.

Section 4.10 **Voting of Deposited Securities.** As soon as practicable after receipt of notice of any meeting at which the holders of Deposited Securities are entitled to vote, or of solicitation of consents or proxies from holders of Deposited Securities, the Depositary shall fix the ADS Record Date in respect of such meeting or solicitation of consent or proxy in accordance with Section 4.9. The Depositary shall, if requested by the Company in writing in a timely manner (the Depositary having no obligation to take any further action if the request shall not have been received by the Depositary at least thirty (30) days prior to the date of such vote or meeting), at the Company's expense and provided no U.S. legal prohibitions exist, distribute as soon as practicable after receipt thereof to Holders as of the ADS Record Date: (a) such notice of meeting or solicitation of consent or proxy, (b) a statement that the Holders at the close of business on the ADS Record Date will be entitled, subject to any applicable law, the provisions of the Deposit Agreement, the Articles of Association of the Company and the provisions of or governing the Deposited Securities (which provisions, if any, shall be summarized in pertinent part by the Company), to instruct the Depositary as to the exercise of the voting rights, if any, pertaining to the Deposited Securities represented by such Holder's ADSs, and (c) a brief statement as to the manner and timing (such timing to be determined after consultation with the Company) in which such voting instructions may be given to the Depositary or in which voting instructions may be deemed to have been given in accordance with this Section 4.10 if no instructions are received prior to the deadline set for such purposes to the Depositary to give a discretionary proxy to a person designated by the Company.

Notwithstanding anything contained in the Deposit Agreement or any ADR, with the Company's prior written consent, the Depositary may, to the extent not prohibited by law or regulations, or by the requirements of any stock exchange on which the ADSs may be listed, in lieu of distribution of the materials provided to the Depositary in connection with any meeting of, or solicitation of consents or proxies from, holders of Deposited Securities, distribute to the Holders a notice that provides Holders with, or otherwise publicize to Holders, instructions on how to retrieve such materials or receive such materials upon request (*e.g.*, by reference to a website containing the materials for retrieval or a contact for requesting copies of the materials).

The Depositary has been advised by the Company that the Articles of Association (as in effect on the date hereof), provide that voting at any meeting of shareholders is by show of hands unless a poll is demanded. The Depositary will not join in demanding a poll, whether or not requested to do so by Holders of ADSs. Under the Articles of Association (as in effect on the date hereof) a poll may be demanded by (i) the chairman of the meeting; (ii) by at least two members of the Company present in person (or by proxy), in each case, for the time being entitled to vote at the meeting; (iii) by any member or members of the Company present in person (or by proxy), in each case, for the time being entitled to vote at the meeting representing at least one-tenth of the total voting rights of all the members having the right to vote at the meeting; or (iv) by any member or members of the Company present in person (or by proxy), in each case, holding shares conferring a right to vote at the meeting, being shares on which an aggregate sum has been paid up equal to at least one-tenth of the total sum paid up on all the shares conferring that right.

Voting instructions may be given only in respect of a number of ADSs representing an integral number of Deposited Securities. Upon the timely receipt from a Holder of ADSs as of the ADS Record Date of voting instructions in the manner specified by the Depositary, the Depositary shall endeavor, insofar as practicable and permitted under any applicable law, the provisions of the Deposit Agreement, the Articles of Association of the Company and the provisions of the Deposited Securities, to vote, or cause the Custodian to vote, the Deposited Securities (in person or by proxy) represented by such Holder's ADSs as follows: (i) in the event voting takes place at a shareholders' meeting by a show of hands, the Depositary will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided voting instructions, and (ii) in the event voting takes place at a shareholders' meeting by poll, the Depositary will instruct the Custodian to vote the Deposited Securities in accordance with the voting instructions received from the Holders of ADSs. If voting is by poll and the Depositary does not receive voting instructions from a Holder as of the ADS Record Date on or before the date established by the Depositary for such purpose, such Holder shall be deemed, and the Depositary shall deem such Holder, to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities; provided, however, that no such discretionary proxy shall be given by the Depositary with respect to any matter to be voted upon as to which the Company informs the Depositary that (a) the Company does not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of Deposited Securities may be adversely affected.

Deposited Securities represented by ADSs for which no timely voting instructions are received by the Depositary from the Holder shall not be voted (except (a) in the case voting is by

show of hands, in which case the Depositary will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided timely voting instructions, and (b) as contemplated in this Section 4.10). Neither the Depositary nor the Custodian shall under any circumstances exercise any discretion as to voting and neither the Depositary nor the Custodian shall vote, attempt to exercise the right to vote, or in any way make use of, for purposes of establishing a quorum or otherwise, the Deposited Securities represented by ADSs, except pursuant to and in accordance with the voting instructions timely received from Holders or as otherwise contemplated herein. If the Depositary timely receives voting instructions from a Holder which fail to specify the manner in which the Depositary is to vote the Deposited Securities represented by such Holder's ADSs, the Depositary will deem such Holder (unless otherwise specified in the notice distributed to Holders) to have instructed the Depositary to vote in favor of the items set forth in such voting instructions.

Notwithstanding anything else contained herein, the Depositary shall, if so requested in writing by the Company, represent all Deposited Securities (whether or not voting instructions have been received in respect of such Deposited Securities from Holders as of the ADS Record Date) for the sole purpose of establishing quorum at a meeting of shareholders.

Notwithstanding anything else contained in the Deposit Agreement or any ADR, the Depositary shall not have any obligation to take any action with respect to any meeting, or solicitation of consents or proxies, of holders of Deposited Securities if the taking of such action would violate U.S. or English laws. The Company agrees to take any and all actions reasonably necessary and as permitted by the laws of England and Wales to enable Holders and Beneficial Owners to exercise the voting rights accruing to the Deposited Securities and to deliver to the Depositary an opinion of U.S. counsel addressing any actions requested to be taken if so requested by the Depositary.

There can be no assurance that Holders generally or any Holder in particular will receive the notice described above with sufficient time to enable the Holder to return voting instructions to the Depositary in a timely manner.

Section 4.11 **Changes Affecting Deposited Securities.** Upon any change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of Deposited Securities, or upon any recapitalization, reorganization, merger, consolidation or sale of assets affecting the Company or to which it is a party, any property which shall be received by the Depositary or the Custodian in exchange for, or in conversion of, or replacement of, or otherwise in respect of, such Deposited Securities shall, to the extent permitted by law, be treated as new Deposited Property under the Deposit Agreement, and the ADSs shall, subject to the provisions of the Deposit Agreement, any ADR(s) evidencing such ADSs and applicable law, represent the right to receive such additional or replacement Deposited Property. In giving effect to such change, split-up, cancellation, consolidation or other reclassification of Deposited Securities, recapitalization, reorganization, merger, consolidation or sale of assets, the Depositary may, with the Company's approval, and shall, if the Company shall so request, subject to the terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary, and (b) applicable taxes) and receipt of an opinion of

counsel to the Company satisfactory to the Depositary that such actions are not in violation of any applicable laws or regulations, (i) issue and deliver additional ADSs as in the case of a stock dividend on the Shares, (ii) amend the Deposit Agreement and the applicable ADRs, (iii) amend the applicable Registration Statement(s) on Form F-6 as filed with the Commission in respect of the ADSs, (iv) call for the surrender of outstanding ADRs to be exchanged for new ADRs, and (v) take such other actions as are appropriate to reflect the transaction with respect to the ADSs. The Company agrees to, jointly with the Depositary, amend the Registration Statement on Form F-6 as filed with the Commission to permit the issuance of such new form of ADRs. Notwithstanding the foregoing, in the event that any Deposited Property so received may not be lawfully distributed to some or all Holders, the Depositary may, with the Company's approval, and shall, if the Company requests, subject to receipt of an opinion of Company's counsel satisfactory to the Depositary that such action is not in violation of any applicable laws or regulations, sell such Deposited Property at public or private sale, at such place or places and upon such terms as it may deem proper and may allocate the net proceeds of such sales (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) for the account of the Holders otherwise entitled to such Deposited Property upon an averaged or other practicable basis without regard to any distinctions among such Holders and distribute the net proceeds so allocated to the extent practicable as in the case of a distribution received in cash pursuant to Section 4.1. The Depositary shall not be responsible for (i) any failure to determine that it may be lawful or practicable to make such Deposited Property available to Holders in general or to any Holder in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or (iii) any liability to the purchaser of such Deposited Property.

Section 4.12 **Available Information.**

The Company is subject to the periodic reporting requirements of the Exchange Act and, accordingly, is required to file or furnish certain reports with the Commission. These reports can be retrieved from the Commission's website (www.sec.gov) and can be inspected and copied at the public reference facilities maintained by the Commission located (as of the date of the Deposit Agreement) at 100 F Street, N.E., Washington D.C. 20549.

Section 4.13 **Reports.** The Depositary shall make available for inspection by Holders at its Principal Office, as promptly as practicable after receipt thereof, any reports and communications, including any proxy soliciting materials, received from the Company which are both (a) received by the Depositary, the Custodian, or the nominee of either of them as the holder of the Deposited Property and (b) made generally available to the holders of such Deposited Property by the Company. The Depositary shall also provide or make available to Holders copies of such reports when furnished by the Company pursuant to Section 5.6.

Section 4.14 **List of Holders.** Promptly upon written request by the Company, the Depositary shall furnish to it a list, as of a recent date, of the names, addresses and holdings of ADSs of all Holders.

Section 4.15 **Taxation**. The Depositary will, and will instruct the Custodian to, forward to the Company or its agents such information from its records as the Company may reasonably request to enable the Company or its agents to file the necessary tax reports with

governmental authorities or agencies. The Depositary, the Custodian or the Company and its agents may file such reports as are necessary to reduce or eliminate applicable taxes on dividends and on other distributions in respect of Deposited Property under applicable tax treaties or laws for the Holders and Beneficial Owners. In accordance with instructions from the Company and to the extent practicable, the Depositary or the Custodian will take reasonable administrative actions to obtain tax refunds, reduced withholding of tax at source on dividends and other benefits under applicable tax treaties or laws with respect to dividends and other distributions on the Deposited Property. As a condition to receiving such benefits, Holders and Beneficial Owners of ADSs may be required from time to time, and in a timely manner, to file such proof of taxpayer status, residence and beneficial ownership (as applicable), to execute such certificates and to make such representations and warranties, or to provide any other information or documents, as the Depositary or the Custodian may deem necessary or proper to fulfill the Depositary's or the Custodian's obligations under applicable law. The Depositary and the Company shall have no obligation or liability to any person if any Holder or Beneficial Owner fails to provide such information or if such information does not reach the relevant tax authorities in time for any Holder or Beneficial Owner to obtain the benefits of any tax treatment. The Holders and Beneficial Owners shall indemnify the Depositary, the Company, the Custodian and any of their respective directors, employees, agents and Affiliates against, and hold each of them harmless from, any claims by any governmental authority with respect to taxes, additions to tax, penalties or interest arising out of any refund of taxes, reduced rate of withholding at source or other tax benefit obtained for that Holder or Beneficial Owner which is required to be paid to such governmental authority.

If the Company (or any of its agents) withholds from any distribution any amount on account of taxes or governmental charges, or pays any other tax in respect of such distribution (*e.g.*, stamp duty tax, capital gains or other similar tax), the Company shall (and shall cause such agent to) remit promptly to the Depositary information about such taxes or governmental charges withheld or paid, and, if so requested, the tax receipt (or other proof of payment to the applicable governmental authority) therefor, in each case, in a form satisfactory to the Depositary. The Depositary shall, to the extent required by U.S. law, report to Holders any taxes withheld by it or the Custodian, and, if such information is provided to it by the Company, any taxes withheld by the Company. The Depositary and the Custodian shall not be required to provide the Holders with any evidence of the remittance by the Company (or its agents) of any taxes withheld, or of the payment of taxes by the Company, except to the extent the evidence is provided by the Company to the Depositary or the Custodian, as applicable. Neither the Depositary nor the Custodian shall be liable for the failure by any Holder or Beneficial Owner to obtain the benefits of credits on the basis of non-U.S. tax paid against such Holder's or Beneficial Owner's income tax liability.

The Depositary is under no obligation to provide the Holders and Beneficial Owners with any information about the tax status of the Company, except to the extent that the Company provides such information to the Depositary for distribution to the Holders and Beneficial Owners. The Depositary shall not incur any liability for any tax consequences that may be incurred by Holders and Beneficial Owners on account of their ownership of the ADSs, including without limitation, tax consequences resulting from the Company (or any of its

subsidiaries) being treated as a "Passive Foreign Investment Company" (in each case as defined in the U.S. Internal Revenue Code and the regulations issued thereunder) or otherwise.

ARTICLE V

THE DEPOSITARY, THE CUSTODIAN AND THE COMPANY

Section 5.1 **Maintenance of Office and Transfer Books by the Registrar.** Until termination of the Deposit Agreement in accordance with its terms, the Registrar shall maintain in the Borough of Manhattan, the City of New York, an office and facilities for the issuance and delivery of ADSs, the acceptance for surrender of ADS(s) for the purpose of withdrawal of Deposited Securities, the registration of issuances, cancellations, transfers, combinations and split-ups of ADS(s) and, if applicable, to countersign ADRs evidencing the ADSs so issued, transferred, combined or split-up, in each case in accordance with the provisions of the Deposit Agreement.

The Registrar shall keep books for the registration of ADSs which at all reasonable times shall be open for inspection by the Company and by the Holders of such ADSs, provided that such inspection shall not be, to the Registrar's knowledge, for the purpose of communicating with Holders of such ADSs in the interest of a business or object other than the business of the Company or other than a matter related to the Deposit Agreement or the ADSs.

The Registrar may close the transfer books with respect to the ADSs, at any time or from time to time, when deemed necessary or advisable by it in good faith in connection with the performance of its duties hereunder, or at the reasonable written request of the Company subject, in all cases, to Section 7.8(a).

If any ADSs are listed on one or more stock exchanges or automated quotation systems in the United States, the Depositary shall act as Registrar or, with written notice given as promptly as practicable to the Company, appoint a Registrar or one or more co-registrars for registration of issuances, cancellations, transfers, combinations and split-ups of ADSs and, if applicable, to countersign ADRs evidencing the ADSs so issued, transferred, combined or split-up, in accordance with any requirements of such exchanges or systems. Such Registrar or co-registrars may be removed and a substitute or substitutes appointed by the Depositary with written notice given as promptly as practicable to the Company.

Section 5.2 **Exoneration.** Notwithstanding anything contained in the Deposit Agreement or any ADR, neither the Depositary nor the Company shall be obligated to do or perform any act which is inconsistent with the provisions of the Deposit Agreement or incur any liability (to the extent not limited by Section 7.8(b)) (i) if the Depositary, the Custodian, the Company or their respective agents shall be prevented or forbidden from, or delayed in, doing or performing any act or thing required or contemplated by the terms of the Deposit Agreement, by reason of any provision of any present or future law or regulation of the United States, England and Wales or any other country, or of any other governmental authority or regulatory authority or stock exchange, or on account of potential criminal or civil penalties or restraint, or by reason of any provision, present or future, of the Articles of Association of the Company or any provision

of or governing any Deposited Securities, or by reason of any act of God or war or other circumstances beyond its control (including, without limitation, nationalization, expropriation, currency restrictions, work stoppage, strikes, civil unrest, acts of terrorism, revolutions, rebellions, explosions and computer failure), (ii) by reason of any exercise of, or failure to exercise, any discretion provided for in the Deposit Agreement or in the Articles of Association of the Company or provisions of or governing Deposited Securities, (iii) for any action or inaction in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Holder, any Beneficial Owner or authorized representative thereof, or any other person believed by it in good faith to be competent to give such advice or information, (iv) for the inability by a Holder or Beneficial Owner to benefit from any distribution, offering, right or other benefit which is made available to holders of Deposited Securities but is not, under the terms of the Deposit Agreement, made available to Holders of ADSs, (v) for any action or inaction of any clearing or settlement system (and any participant thereof) for the Deposited Property or the ADSs, or (vi) for any consequential or punitive damages (including lost profits) for any breach of the terms of the Deposit Agreement.

The Depositary, its controlling persons, its agents, any Custodian and the Company, its controlling persons and its agents may rely and shall be protected in acting upon any written notice, request or other document believed by it to be genuine and to have been signed or presented by the proper party or parties.

Section 5.3 **Standard of Care.** The Company and the Depositary assume no obligation and shall not be subject to any liability under the Deposit Agreement or any ADRs to any Holder(s) or Beneficial Owner(s), except that the Company and the Depositary agree to perform their respective obligations specifically set forth in the Deposit Agreement or the applicable ADRs without negligence or bad faith.

Without limitation of the foregoing, neither the Depositary, nor the Company, nor any of their respective controlling persons, or agents, shall be under any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Property or in respect of the ADSs, which in its opinion may involve it in expense or liability, unless indemnity satisfactory to it against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be required (and no Custodian shall be under any obligation whatsoever with respect to such proceedings, the responsibility of the Custodian being solely to the Depositary).

The Depositary and its agents shall not be liable for any failure to carry out any instructions to vote any of the Deposited Securities, or for the manner in which any vote is cast or the effect of any vote, provided that any such action or omission is in good faith and without negligence and in accordance with the terms of the Deposit Agreement. The Depositary shall not incur any liability for any failure to accurately determine that any distribution or action may be lawful or reasonably practicable, for the content of any information submitted to it by the Company for distribution to the Holders or for any inaccuracy of any translation thereof, for any investment risk associated with acquiring an interest in the Deposited Property, for the validity or worth of the Deposited Property, for the value of any Deposited Property or any distribution thereon, for any interest on Deposited Property, for any tax consequences that may result from

the ownership of ADSs, Shares or other Deposited Property, for the credit-worthiness of any third party, for allowing any rights to lapse upon the terms of the Deposit Agreement, for the failure or timeliness of any notice from the Company, or for any action of or failure to act by, or any information provided or not provided by, DTC or any DTC Participant.

The Depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the Depositary or in connection with any matter arising wholly after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises the Depositary performed its obligations without negligence or bad faith while it acted as Depositary for the Company.

Section 5.4 **Resignation and Removal of the Depositary; Appointment of Successor Depositary.** The Depositary may at any time resign as Depositary hereunder by written notice of resignation delivered to the Company, such resignation to be effective on the earlier of (i) the 90th day after delivery thereof to the Company (whereupon the Depositary shall be entitled to take the actions contemplated in Section 6.2), or (ii) the appointment by the Company of a successor depositary and its acceptance of such appointment as hereinafter provided.

The Depositary may at any time be removed by the Company by written notice of such removal, which removal shall be effective on the later of (i) the 90th day after delivery thereof to the Depositary (whereupon the Depositary shall be entitled to take the actions contemplated in Section 6.2), or (ii) upon the appointment by the Company of a successor depositary and its acceptance of such appointment as hereinafter provided.

In case at any time the Depositary acting hereunder shall resign or be removed, the Company shall use its best efforts to appoint a successor depositary, which shall be a bank or trust company having an office in the Borough of Manhattan, the City of New York. Every successor depositary shall be required by the Company to execute and deliver to its predecessor and to the Company an instrument in writing accepting its appointment hereunder, and thereupon such successor depositary, without any further act or deed (except as required by applicable law), shall become fully vested with all the rights, powers, duties and obligations of its predecessor (other than as contemplated in Sections 5.8 and 5.9). The predecessor depositary, upon payment of all sums due it and on the written request of the Company, shall, (i) execute and deliver an instrument transferring to such successor all rights and powers of such predecessor hereunder (other than as contemplated in Sections 5.8 and 5.9), (ii) duly assign, transfer and deliver all of the Depositary's right, title and interest to the Deposited Property to such successor, and (iii) deliver to such successor a list of the Holders of all outstanding ADSs and such other information relating to ADSs and Holders thereof as the successor may reasonably request. Any such successor depositary shall promptly provide notice of its appointment to such Holders.

Any entity into or with which the Depositary may be merged or consolidated shall be the successor of the Depositary without the execution or filing of any document or any further act.

Section 5.5 **The Custodian.** The Depositary has initially appointed Citibank, N.A. (London) as Custodian for the purpose of the Deposit Agreement. The Custodian or its successors in acting hereunder shall be authorized to act as custodian in England and Wales and shall be subject at all times and in all respects to the direction of the Depositary for the Deposited Property for which the Custodian acts as custodian and shall be responsible solely to it. If any Custodian resigns or is discharged from its duties hereunder with respect to any Deposited Property and no other Custodian has previously been appointed hereunder, the Depositary shall promptly appoint a substitute custodian. The Depositary shall require such resigning or discharged Custodian to Deliver, or cause the Delivery of, the Deposited Property held by it, together with all such records maintained by it as Custodian with respect to such Deposited Property as the Depositary may request, to the Custodian designated by the Depositary. Whenever the Depositary determines, in its discretion, that it is appropriate to do so, it may appoint an additional custodian with respect to any Deposited Property, or discharge the Custodian with respect to any Deposited Property and appoint a substitute custodian, which shall thereafter be Custodian hereunder with respect to the Deposited Property. Immediately upon any such change, the Depositary shall give notice thereof in writing to all Holders of ADSs, each other Custodian and the Company.

Citibank may at any time act as Custodian of the Deposited Property pursuant to the Deposit Agreement, in which case any reference to Custodian shall mean Citibank solely in its capacity as Custodian pursuant to the Deposit Agreement and the Depositary shall promptly give notice thereof to the Company. Notwithstanding anything contained in the Deposit Agreement or any ADR, the Depositary shall not be obligated to give notice to any Holders of ADSs or any other Custodian of its acting as Custodian pursuant to the Deposit Agreement.

Upon the appointment of any successor depositary, any Custodian then acting hereunder shall, unless otherwise instructed by the Depositary, continue to be the Custodian of the Deposited Property without any further act or writing, and shall be subject to the direction of the successor depositary. The successor depositary so appointed shall, nevertheless, on the written request of any Custodian, execute and deliver to such Custodian all such instruments as may be proper to give to such Custodian full and complete power and authority to act on the direction of such successor depositary.

Section 5.6 **Notices and Reports.** On or before the first date on which the Company gives notice, by publication or otherwise, of any meeting of holders of Shares or other Deposited Securities, or of any adjourned meeting of such holders, or of the taking of any action by such holders other than at a meeting, or of the taking of any action in respect of any cash or other distributions or the offering of any rights in respect of Deposited Securities, the Company shall transmit to the Depositary and the Custodian a copy of the notice thereof in the English language but otherwise in the form given or to be given to holders of Shares or other Deposited Securities. The Company shall also furnish to the Custodian and the Depositary a summary, in English, of any applicable provisions or proposed provisions of the Articles of Association of the Company that may be relevant or pertain to such notice of meeting or be the subject of a vote thereat.

The Depositary shall arrange, at the request of the Company and at the Company’s expense, to provide copies thereof to all Holders or make such notices, reports and other

communications available to all Holders on a basis similar to that for holders of Shares or other Deposited Securities or on such other basis as the Company may advise the Depositary or as may be required by any applicable law, regulation or stock exchange requirement. The Company has delivered to the Depositary and the Custodian a copy of the Company's Articles of Association along with the provisions of or governing the Shares and any other Deposited Securities issued by the Company in connection with such Shares, and promptly upon any amendment thereto or change therein, the Company shall deliver to the Depositary and the Custodian a copy of such amendment thereto or change therein to the extent such amendment or change is not available on the Company's website or is not otherwise publicly available. The Depositary may rely upon such copy for all purposes of the Deposit Agreement.

The Depositary will, at the expense of the Company, make available a copy of any such notices, reports or communications issued by the Company and delivered to the Depositary for inspection by the Holders of the ADSs at the Depositary's Principal Office, at the office of the Custodian and at any other designated transfer office.

Section 5.7 **Issuance of Additional Shares, ADSs etc.** The Company agrees that in the event it or any of its Affiliates proposes (i) an issuance, sale or distribution of additional Shares, (ii) an offering of rights to subscribe for Shares or other Deposited Securities, (iii) an issuance or assumption of securities convertible into or exchangeable for Shares, (iv) an issuance of rights to subscribe for securities convertible into or exchangeable for Shares, (v) an elective dividend of cash or Shares, (vi) a redemption of Deposited Securities, (vii) a meeting of holders of Deposited Securities, or solicitation of consents or proxies, relating to any reclassification of securities, merger or consolidation or transfer of assets, (viii) any assumption, reclassification, recapitalization, reorganization, merger, consolidation or sale of assets which affects the Deposited Securities, or (ix) a distribution of securities other than Shares, it will obtain U.S. legal advice and take all steps necessary to ensure that the application of the proposed transaction to Holders and Beneficial Owners does not violate the registration provisions of the Securities Act, or any other applicable laws (including, without limitation, the Investment Company Act of 1940, as amended, the Exchange Act and the securities laws of the states of the U.S.). In support of the foregoing, the Company will furnish to the Depositary (a) a written opinion of U.S. counsel (reasonably satisfactory to the Depositary) stating whether such transaction (1) requires a registration statement under the Securities Act to be in effect or (2) is exempt from the registration requirements of the Securities Act and (b) an opinion of English counsel stating that (1) making the transaction available to Holders and Beneficial Owners does not violate the laws or regulations of England and Wales and (2) all requisite regulatory consents and approvals have been obtained in England and Wales. If the filing of a registration statement is required, the Depositary shall not have any obligation to proceed with the transaction unless it shall have received evidence reasonably satisfactory to it that such registration statement has been declared effective. If, being advised by counsel, the Company determines that a transaction is required to be registered under the Securities Act, the Company will either (i) register such transaction to the extent necessary, (ii) alter the terms of the transaction to avoid the registration requirements of the Securities Act or (iii) direct the Depositary to take specific measures, in each case as contemplated in the Deposit Agreement, to prevent such transaction from violating the registration requirements of the Securities Act. The Company agrees with the Depositary that neither the Company nor any of its Affiliates will at any time (i) deposit any Shares or other

Deposited Securities, either upon original issuance or upon a sale of Shares or other Deposited Securities previously issued and reacquired by the Company or by any such Affiliate, or (ii) issue additional Shares, rights to subscribe for such Shares, securities convertible into or exchangeable for Shares or rights to subscribe for such securities or distribute securities other than Shares, unless such transaction and the securities issuable in such transaction do not violate the registration provisions of the Securities Act, or any other applicable laws (including, without limitation, the Investment Company Act of 1940, as amended, the Exchange Act and the securities laws of the states of the U.S.).

Notwithstanding anything else contained in the Deposit Agreement, nothing in the Deposit Agreement shall be deemed to obligate the Company to file any registration statement in respect of any proposed transaction.

Section 5.8 **Indemnification.** The Depositary agrees to indemnify the Company and its directors, officers, employees, agents and Affiliates against, and hold each of them harmless from, any direct loss, liability, tax, charge or expense of any kind whatsoever (including, but not limited to, the reasonable fees and expenses of counsel) which may arise out of acts performed or omitted by the Depositary under the terms hereof due to the negligence or bad faith of the Depositary.

The Company agrees to indemnify the Depositary, the Custodian and any of their respective directors, officers, employees, agents and Affiliates against, and hold each of them harmless from, any direct loss, liability, tax, charge or expense of any kind whatsoever (including, but not limited to, the reasonable fees and expenses of counsel) that may arise (a) out of, or in connection with, any offer, issuance, sale, resale, transfer, deposit or withdrawal of ADRs, ADSs, the Shares, or other Deposited Securities, as the case may be, to the extent it is not unlawful for the Company to indemnify such person at such time under applicable English law, (b) out of, or as a result of, any offering documents in respect thereof or (c) out of acts performed or omitted, including, but not limited to, any delivery by the Depositary on behalf of the Company of information regarding the Company, in connection with the Deposit Agreement, any ancillary or supplemental agreement entered into between the Company and the Depositary, the ADRs, the ADSs, the Shares, or any Deposited Property, in any such case (i) by the Depositary, the Custodian or any of their respective directors, officers, employees, agents and Affiliates, except to the extent such loss, liability, tax, charge or expense is due to the fraud, negligence or bad faith of any of them, or (ii) by the Company or any of its directors, officers, employees, agents and Affiliates; provided. However, that the Company shall not be liable for any fees, charges or expenses payable by third party Holders or Beneficial Owners under this Deposit Agreement. The Company shall not indemnify the Depositary or the Custodian (for so long as the Custodian is a branch of Citibank, N.A.) against any liability or expense arising out of information relating to the Depositary or such Custodian, as the case may be, furnished in a signed writing to the Company, executed by the Depositary expressly for use in any registration statement, prospectus or preliminary prospectus relating to any Deposited Securities represented by the ADSs.

The obligations set forth in this Section shall survive the termination of the Deposit Agreement and the succession or substitution of any party hereto.

Any person seeking indemnification hereunder (an "indemnified person") shall notify the person from whom it is seeking indemnification (the "indemnifying person") of the commencement of any indemnifiable action or claim promptly after such indemnified person becomes aware of such commencement (provided that the failure to make such notification shall not affect such indemnified person's rights to seek indemnification except to the extent the indemnifying person is materially prejudiced by such failure) and shall consult in good faith with the indemnifying person as to the conduct of the defense of such action or claim that may give rise to an indemnity hereunder, which defense shall be reasonable in the circumstances. No indemnified person shall compromise or settle any action or claim that may give rise to an indemnity hereunder without the consent of the indemnifying person, which consent shall not be unreasonably withheld.

Section 5.9 **ADS Fees and Charges**. The Company, the Holders, the Beneficial Owners, persons depositing Shares or withdrawing Deposited Securities in connection with the issuance and cancellation of ADSs, and persons receiving ADSs upon issuance or for whom ADSs are being cancelled shall be required to pay the ADS fees and charges identified as payable by them respectively in the Fee Schedule attached hereto as Exhibit B. All ADS fees and charges so payable may be deducted from distributions or must be remitted to the Depositary, or its designee, and may, at any time and from time to time, be changed by agreement between the Depositary and the Company, but, in the case of ADS fees and charges payable by Holders and Beneficial Owners, only in the manner contemplated in Section 6.1. The Depositary shall provide, without charge, a copy of its latest ADS fee schedule to anyone upon request.

ADS fees and charges payable upon (i) the issuance of ADSs and (ii) the cancellation of ADSs will be payable by the person for whom the ADSs are so issued by the Depositary (in the case of ADS issuances) and by the person for whom ADSs are being cancelled by the Depositary (in the case of ADS cancellations). In the case of ADSs issued by the Depositary into DTC or presented to the Depositary via DTC, the ADS issuance and cancellation fees and charges will be payable by the DTC Participant(s) receiving the ADSs from the Depositary or the DTC Participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the Beneficial Owner(s) and will be charged by the DTC Participant(s) to the account(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC Participant(s) as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are payable by Holders as of the applicable ADS Record Date established by the Depositary. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, the applicable Holders as of the ADS Record Date established by the Depositary will be invoiced for the amount of the ADS fees and charges and such ADS fees may be deducted from distributions made to Holders. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC Participants in accordance with the procedures and practices prescribed by DTC from time to time and the DTC Participants in turn charge the amount of such ADS fees and charges to the Beneficial Owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the ADS Holder whose ADSs are being transferred or by the person to whom

the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the Holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to the Deposit Agreement, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges, and reimburse the Depositary for such out-of-pocket expenses, as the Depositary and the Company may agree from time to time. Responsibility for payment of such fees, charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such fees, charges and reimbursements to the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary.

The obligations of Holders and Beneficial Owners to pay ADS fees and charges shall survive the termination of the Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in Section 5.4, the right to collect ADS fees and charges shall extend for those ADS fees and charges incurred prior to the effectiveness of such resignation or removal.

Section 5.10 **Restricted Securities Owners.** The Company agrees to advise in writing each of the persons or entities who, to the knowledge of the Company, holds Restricted Securities that such Restricted Securities are ineligible for deposit hereunder (except under the circumstances contemplated in Section 2.14) and, to the extent practicable, shall require each of such persons to represent in writing that such person will not deposit Restricted Securities hereunder (except under the circumstances contemplated in Section 2.14).

ARTICLE VI

AMENDMENT AND TERMINATION

Section 6.1 **Amendment/Supplement.** Subject to the terms and conditions of this Section 6.1 and applicable law, the ADRs outstanding at any time, the provisions of the Deposit Agreement and the form of ADR attached hereto and to be issued under the terms hereof may at any time and from time to time be amended or supplemented by written agreement between the Company and the Depositary in any respect which they may deem necessary or desirable without the prior written consent of the Holders or Beneficial Owners. Any amendment or supplement which shall impose or increase any fees or charges (other than charges in connection with foreign exchange control regulations, and taxes and other governmental charges, delivery and other such expenses), or which shall otherwise materially prejudice any substantial existing right of Holders or Beneficial Owners, shall not, however, become effective as to outstanding ADSs until the expiration of thirty (30) days after notice of such amendment or supplement shall have been given to the Holders of outstanding ADSs. Notice of any amendment to the Deposit Agreement or any ADR shall not need to describe in detail the specific amendments effectuated

thereby, and failure to describe the specific amendments in any such notice shall not render such notice invalid, provided, however, that, in each such case, the notice given to the Holders identifies a means for Holders and Beneficial Owners to retrieve or receive the text of such amendment (*e.g.*, upon retrieval from the Commission's, the Depositary's or the Company's website or upon request from the Depositary). The parties hereto agree that any amendments or supplements which (i) are reasonably necessary (as agreed by the Company and the Depositary) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act or (b) the ADSs to be settled solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by Holders, shall be deemed not to materially prejudice any substantial rights of Holders or Beneficial Owners. Every Holder and Beneficial Owner at the time any amendment or supplement so becomes effective shall be deemed, by continuing to hold such ADSs, to consent and agree to such amendment or supplement and to be bound by the Deposit Agreement and the ADR, if applicable, as amended or supplemented thereby. In no event shall any amendment or supplement impair the right of the Holder to surrender such ADS and receive therefor the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law. Notwithstanding the foregoing, if any governmental body should adopt new laws, rules or regulations which would require an amendment of, or supplement to, the Deposit Agreement to ensure compliance therewith, the Company and the Depositary may amend or supplement the Deposit Agreement and any ADRs at any time in accordance with such changed laws, rules or regulations. Such amendment or supplement to the Deposit Agreement and any ADRs in such circumstances may become effective before a notice of such amendment or supplement is given to Holders or within any other period of time as required for compliance with such laws, rules or regulations.

Section 6.2 Termination. The Depositary shall, at any time at the written direction of the Company, terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. If ninety (90) days shall have expired after (i) the Depositary shall have delivered to the Company a written notice of its election to resign, or (ii) the Company shall have delivered to the Depositary a written notice of the removal of the Depositary, and, in either case, a successor depositary shall not have been appointed and accepted its appointment as provided in Section 5.4 of the Deposit Agreement, the Depositary may terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. The date so fixed for termination of the Deposit Agreement in any termination notice so distributed by the Depositary to the Holders of ADSs is referred to as the "Termination Date". Until the Termination Date, the Depositary shall continue to perform all of its obligations under the Deposit Agreement, and the Holders and Beneficial Owners will be entitled to all of their rights under the Deposit Agreement.

If any ADSs shall remain outstanding after the Termination Date, the Registrar and the Depositary shall not, after the Termination Date, have any obligation to perform any further acts under the Deposit Agreement, except that the Depositary shall, subject, in each case, to the terms and conditions of the Deposit Agreement, continue to (i) collect dividends and other distributions pertaining to Deposited Securities, (ii) sell Deposited Property received in respect of Deposited Securities, (iii) deliver Deposited Securities, together with any dividends or other distributions

received with respect thereto and the net proceeds of the sale of any other Deposited Property, in exchange for ADSs surrendered to the Depositary (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (iv) take such actions as may be required under applicable law in connection with its role as Depositary under the Deposit Agreement.

At any time after the Termination Date, the Depositary may sell the Deposited Property then held under the Deposit Agreement and shall after such sale hold un-invested the net proceeds of such sale, together with any other cash then held by it under the Deposit Agreement, in an un-segregated account and without liability for interest, for the pro rata benefit of the Holders whose ADSs have not theretofore been surrendered. After making such sale, the Depositary shall be discharged from all obligations under the Deposit Agreement except (i) to account for such net proceeds and other cash (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (ii) as may be required at law in connection with the termination of the Deposit Agreement. After the Termination Date, the Company shall be discharged from all obligations under the Deposit Agreement, except for its obligations to the Depositary under Sections 5.8, 5.9 and 7.6 of the Deposit Agreement. The obligations under the terms of the Deposit Agreement of Holders and Beneficial Owners of ADSs outstanding as of the Termination Date shall survive the Termination Date and shall be discharged only when the applicable ADSs are presented by their Holders to the Depositary for cancellation under the terms of the Deposit Agreement (except as specifically provided in the Deposit Agreement).

Notwithstanding anything contained in the Deposit Agreement or any ADR, in connection with the termination of the Deposit Agreement, the Depositary may, independently and without the need for any action by the Company, make available to Holders of ADSs a means to withdraw the Deposited Securities represented by their ADSs and to direct the deposit of such Deposited Securities into an unsponsored American depositary shares program established by the Depositary, upon such terms and conditions as the Depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored American depositary shares program under the Securities Act, and to receipt by the Depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the Depositary.

ARTICLE VII

MISCELLANEOUS

Section 7.1 **Counterparts.** The Deposit Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of such counterparts together shall constitute one and the same agreement. Copies of the Deposit Agreement shall be

maintained with the Depositary and shall be open to inspection by any Holder during business hours.

Section 7.2 **No Third-Party Beneficiaries/Acknowledgments.** The Deposit Agreement is for the exclusive benefit of the parties hereto (and their successors) and shall not be deemed to give any legal or equitable right, remedy or claim whatsoever to any other person, except to the extent specifically set forth in the Deposit Agreement. Nothing in the Deposit Agreement shall be deemed to give rise to a partnership or joint venture among the parties nor establish a fiduciary or similar relationship among the parties. The parties hereto acknowledge and agree that (i) Citibank and its Affiliates may at any time have multiple banking relationships with the Company, the Holders, the Beneficial Owners, and their respective Affiliates, (ii) Citibank and its Affiliates may own and deal in any class of securities of the Company and its Affiliates and in ADSs, and may be engaged at any time in transactions in which parties adverse to the Company, the Holders, the Beneficial Owners or their respective Affiliates may have interests, (iii) the Depositary and its Affiliates may from time to time have in their possession non-public information about the Company, the Holders, the Beneficial Owners, and their respective Affiliates, (iv) nothing contained in the Deposit Agreement shall (a) preclude Citibank or any of its Affiliates from engaging in such transactions or establishing or maintaining such relationships, or (b) obligate Citibank or any of its Affiliates to disclose such information, transactions or relationships, or to account for any profit made or payment received in such transactions or relationships, (v) the Depositary shall not be deemed to have knowledge of any information any other division of Citibank or any of its Affiliates may have about the Company, the Holders, the Beneficial Owners, or any of their respective Affiliates, and (vi) the Company, the Depositary, the Custodian and their respective agents and controlling persons may be subject to the laws and regulations of jurisdictions other than the United States, England, and the authority of courts and regulatory authorities of such other jurisdictions, and, consequently, the requirements and the limitations of such other laws and regulations, and the decisions and orders of such other courts and regulatory authorities, may affect the rights and obligations of the parties to the Deposit Agreement.

Section 7.3 **Severability.** In case any one or more of the provisions contained in the Deposit Agreement or in the ADRs should be or become invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein or therein shall in no way be affected, prejudiced or disturbed thereby.

Section 7.4 **Holders and Beneficial Owners as Parties; Binding Effect.** The Holders and Beneficial Owners from time to time of ADSs issued hereunder shall be parties to the Deposit Agreement and shall be bound by all of the terms and conditions hereof and of any ADR evidencing their ADSs by acceptance thereof or any beneficial interest therein.

Section 7.5 **Notices.** Any and all notices to be given to the Company shall be deemed to have been duly given if personally delivered or sent by mail, air courier or cable, telex or facsimile transmission, confirmed by letter personally delivered or sent by mail or air courier, addressed to Bicycle Therapeutics plc, B900, Babraham Research Campus, Cambridge CB22 3AT, United Kingdom, Attention: Lee Kalowski, Chief Financial Officer, or to any other address which the Company may specify in writing to the Depositary.

Any and all notices to be given to the Depositary shall be deemed to have been duly given if personally delivered or sent by mail, air courier or cable, telex or facsimile transmission, confirmed by letter personally delivered or sent by mail or air courier, addressed to Citibank, N.A., 388 Greenwich Street, New York, New York 10013, U.S.A., Attention: Depositary Receipts Department, or to any other address which the Depositary may specify in writing to the Company.

Any and all notices to be given to any Holder shall be deemed to have been duly given **(a)** if personally delivered or sent by mail or cable, telex or facsimile transmission, confirmed by letter, addressed to such Holder at the address of such Holder as it appears on the books of the Depositary or, if such Holder shall have filed with the Depositary a request that notices intended for such Holder be mailed to some other address, at the address specified in such request, or **(b)** if a Holder shall have designated such means of notification as an acceptable means of notification under the terms of the Deposit Agreement, by means of electronic messaging addressed for delivery to the e-mail address designated by the Holder for such purpose. Notice to Holders shall be deemed to be notice to Beneficial Owners for all purposes of the Deposit Agreement. Failure to notify a Holder or any defect in the notification to a Holder shall not affect the sufficiency of notification to other Holders or to the Beneficial Owners of ADSs held by such other Holders. Any notices given to DTC under the terms of the Deposit Agreement shall (unless otherwise specified by the Depositary) constitute notice to the DTC Participants who hold the ADSs in their DTC accounts and to the Beneficial Owners of such ADSs.

Delivery of a notice sent by mail, air courier or cable, telex or facsimile transmission shall be deemed to be effective at the time when a duly addressed letter containing the same (or a confirmation thereof in the case of a cable, telex or facsimile transmission) is deposited, postage prepaid, in a post-office letter box or delivered to an air courier service, without regard for the actual receipt or time of actual receipt thereof by a Holder. The Depositary or the Company may, however, act upon any cable, telex or facsimile transmission received by it from any Holder, the Custodian, the Depositary, or the Company, notwithstanding that such cable, telex or facsimile transmission shall not be subsequently confirmed by letter.

Delivery of a notice by means of electronic messaging shall be deemed to be effective at the time of the initiation of the transmission by the sender (as shown on the sender's records), notwithstanding that the intended recipient retrieves the message at a later date, fails to retrieve such message, or fails to receive such notice on account of its failure to maintain the designated e-mail address, its failure to designate a substitute e-mail address or for any other reason.

Section 7.6 **Governing Law and Jurisdiction.** The Deposit Agreement, the ADRs and the ADSs shall be interpreted in accordance with, and all rights hereunder and thereunder and provisions hereof and thereof shall be governed by, the laws of the State of New York applicable to contracts made and to be wholly performed in that State. Notwithstanding anything contained in the Deposit Agreement, any ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and the obligations and duties of the Company in respect of the holders of Shares and other Deposited Securities, as such, shall be governed by the laws of England and Wales (or, if applicable, such other laws as may govern the Deposited Securities).

Except as set forth in the following paragraph of this Section 7.6, the Company and the Depositary agree that the federal or state courts in the City of New York shall have jurisdiction to hear and determine any suit, action or proceeding and to settle any dispute between them that may arise out of or in connection with the Deposit Agreement and, for such purposes, each irrevocably submits to the non-exclusive jurisdiction of such courts. The Company hereby irrevocably designates, appoints and empowers Computershare Investor Services plc (the "Agent") now at [**Address of Computershare Investor Services plc**] as its authorized agent to receive and accept for and on its behalf, and on behalf of its properties, assets and revenues, service by mail of any and all legal process, summons, notices and documents that may be served in any suit, action or proceeding brought against the Company in any federal or state court as described in the preceding sentence or in the next paragraph of this Section 7.6. If for any reason the Agent shall cease to be available to act as such, the Company agrees to designate a new agent in New York on the terms and for the purposes of this Section 7.6 reasonably satisfactory to the Depositary. The Company further hereby irrevocably consents and agrees to the service of any and all legal process, summons, notices and documents in any suit, action or proceeding against the Company, by service by mail of a copy thereof upon the Agent (whether or not the appointment of such Agent shall for any reason prove to be ineffective or such Agent shall fail to accept or acknowledge such service), with a copy mailed to the Company by registered or certified air mail, postage prepaid, to its address provided in Section 7.5. The Company agrees that the failure of the Agent to give any notice of such service to it shall not impair or affect in any way the validity of such service or any judgment rendered in any action or proceeding based thereon.

Notwithstanding the foregoing, the Depositary and the Company unconditionally agree that in the event that a Holder or Beneficial Owner brings a suit, action or proceeding against (a) the Company, (b) the Depositary in its capacity as Depositary under the Deposit Agreement, or (c) against both the Company and the Depositary, in any such case, in any state or federal court of the United States, and the Depositary or the Company have any claim, for indemnification or otherwise, against each other arising out of the subject matter of such suit, action or proceeding, then the Company and the Depositary may pursue such claim against each other in the state or federal court in the United States in which such suit, action, or proceeding is pending and, for such purposes, the Company and the Depositary irrevocably submit to the non-exclusive jurisdiction of such courts. The Company agrees that service of process upon the Agent in the manner set forth in the preceding paragraph shall be effective service upon it for any suit, action or proceeding brought against it as described in this paragraph.

The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of venue of any actions, suits or proceedings brought in any court as provided in this Section 7.6, and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum.

The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, and agrees not to plead or claim, any right of immunity from legal action, suit or proceeding, from setoff or counterclaim, from the jurisdiction of any court, from service of

process, from attachment upon or prior to judgment, from attachment in aid of execution or judgment, from execution of judgment, or from any other legal process or proceeding for the giving of any relief or for the enforcement of any judgment, and consents to such relief and enforcement against it, its assets and its revenues in any jurisdiction, in each case with respect to any matter arising out of, or in connection with, the Deposit Agreement, any ADR or the Deposited Property.

EACH OF THE PARTIES TO THE DEPOSIT AGREEMENT (INCLUDING, WITHOUT LIMITATION, EACH HOLDER AND BENEFICIAL OWNER) IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING AGAINST THE COMPANY AND/OR THE DEPOSITARY ARISING OUT OF, OR RELATING TO, THE DEPOSIT AGREEMENT, ANY ADR AND ANY TRANSACTIONS CONTEMPLATED THEREIN (WHETHER BASED ON CONTRACT, TORT, COMMON LAW OR OTHERWISE).

The provisions of this Section 7.6 shall survive any termination of the Deposit Agreement, in whole or in part.

Section 7.7 **Assignment.** Subject to the provisions of Section 5.4, the Deposit Agreement may not be assigned by either the Company or the Depositary.

Section 7.8 **Compliance with, and No Disclaimer under, U.S. Securities Laws.**

(a) Notwithstanding anything in the Deposit Agreement to the contrary, the withdrawal or delivery of Deposited Securities will not be suspended by the Company or the Depositary except as would be permitted by Instruction I.A.(1) of the General Instructions to Form F-6 Registration Statement, as amended from time to time, under the Securities Act.

(b) Each of the parties to the Deposit Agreement (including, without limitation, each Holder and Beneficial Owner) acknowledges and agrees that no provision of the Deposit Agreement or any ADR shall, or shall be deemed to, disclaim any liability under the Securities Act or the Exchange Act, in each case to the extent established under applicable U.S. laws.

Section 7.9 **English Law References.** Any summary of English laws and regulations and of the terms of the Company's Articles of Association set forth in the Deposit Agreement have been provided by the Company solely for the convenience of Holders, Beneficial Owners and the Depositary. While such summaries are believed by the Company to be accurate as of the date of the Deposit Agreement, (i) they are summaries and as such may not include all aspects of the materials summarized applicable to a Holder or Beneficial Owner, and (ii) these laws and regulations and the Company's Articles of Association may change after the date of the Deposit Agreement. Neither the Depositary nor the Company has any obligation under the terms of the Deposit Agreement to update any such summaries.

Section 7.10 Titles and References.

(a) Deposit Agreement. All references in the Deposit Agreement to exhibits, articles, sections, subsections, and other subdivisions refer to the exhibits, articles, sections, subsections and other subdivisions of the Deposit Agreement unless expressly provided otherwise. The words "the Deposit Agreement", "herein", "hereof", "hereby", "hereunder", and words of similar import refer to the Deposit Agreement as a whole as in effect at the relevant time between the Company, the Depositary and the Holders and Beneficial Owners of ADSs and not to any particular subdivision unless expressly so limited. Pronouns in masculine, feminine and neuter gender shall be construed to include any other gender, and words in the singular form shall be construed to include the plural and *vice versa* unless the context otherwise requires. Titles to sections of the Deposit Agreement are included for convenience only and shall be disregarded in construing the language contained in the Deposit Agreement. References to "applicable laws and regulations" shall refer to laws and regulations applicable to ADRs, ADSs or Deposited Property as in effect at the relevant time of determination, unless otherwise required by law or regulation.

(b) ADRs. All references in any ADR(s) to paragraphs, exhibits, articles, sections, subsections, and other subdivisions refer to the paragraphs, exhibits, articles, sections, subsections and other subdivisions of the ADR(s) in question unless expressly provided otherwise. The words "the Receipt", "the ADR", "herein", "hereof", "hereby", "hereunder", and words of similar import used in any ADR refer to the ADR as a whole and as in effect at the relevant time, and not to any particular subdivision unless expressly so limited. Pronouns in masculine, feminine and neuter gender in any ADR shall be construed to include any other gender, and words in the singular form shall be construed to include the plural and *vice versa* unless the context otherwise requires. Titles to paragraphs of any ADR are included for convenience only and shall be disregarded in construing the language contained in the ADR. References to "applicable laws and regulations" shall refer to laws and regulations applicable to the Company, the Depositary, the Custodian, their agents and controlling persons, the ADRs, the ADSs and the Deposited Property as in effect at the relevant time of determination, unless otherwise required by law or regulation.

[*Signature Page to Follow]*

IN WITNESS WHEREOF, BICYCLE THERAPEUTICS PLC and CITIBANK, N.A. have duly executed the Deposit Agreement as of the day and year first above set forth and all Holders and Beneficial Owners shall become parties hereto upon acceptance by them of ADSs issued in accordance with the terms hereof, or upon acquisition of any beneficial interest therein.

BICYCLE THERAPEUTICS PLC

By: _____
Name:
Title:

CITIBANK, N.A.

By: _____
Name:
Title:

EXHIBIT A

[FORM OF ADR]

Number CUSIP NUMBER:

American Depositary Shares (each American Depositary Share representing the right to receive **[number of shares]** fully paid ordinary shares)

AMERICAN DEPOSITARY RECEIPT

for

AMERICAN DEPOSITARY SHARES

representing

DEPOSITED ORDINARY SHARES

of

Bicycle Therapeutics plc

(Incorporated under the laws of England and Wales)

CITIBANK, N.A., a national banking association organized and existing under the laws of the United States of America, as depositary (the "Depositary"), hereby certifies that is the owner of American Depositary Shares (hereinafter "ADS") representing deposited ordinary shares, including evidence of rights to receive such ordinary shares (the "Shares"), of Bicycle Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the "Company"). As of the date of issuance of this ADR, each ADS represents the right to receive **[number of shares]** Shares deposited under the Deposit Agreement (as hereinafter defined) with the Custodian, which at the date of issuance of this ADR is Citibank, N.A. (London) (the "Custodian"). The ADS(s)-to-Share(s) ratio is subject to amendment as provided in Articles IV and VI of the Deposit Agreement. The Depositary's Principal Office is located at 388 Greenwich Street, New York, New York 10013, U.S.A.

(1) **The Deposit Agreement.** This American Depositary Receipt is one of an issue of American Depositary Receipts ("ADRs"), all issued and to be issued upon the terms and conditions set forth in theDeposit Agreement, dated as of **[date]**, 2019 (as amended and supplemented from time to time, the "Deposit Agreement"), by and among the Company, the Depositary, and all Holders and Beneficial Owners from time to time of ADSs issued thereunder. The Deposit Agreement sets forth the rights and obligations of Holders and Beneficial Owners of ADSs and the rights and duties of the Depositary in respect of the Shares deposited thereunder and any and all other Deposited Property (as defined in the Deposit Agreement) from time to time received and held on deposit in respect of the ADSs. Copies of the Deposit Agreement are on file at the Principal Office of the Depositary and with the Custodian. Each Holder and each Beneficial Owner, upon acceptance of any ADSs (or any interest therein) issued in accordance with the terms and conditions of the Deposit Agreement, shall be deemed for all purposes to (a) be a party to and bound by the terms of the Deposit Agreement and the applicable ADR(s), and (b) appoint the Depositary its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in the Deposit Agreement and the applicable ADR(s), to adopt any and all procedures necessary to comply with applicable law and to take such action as the Depositary in its sole discretion may deem necessary or appropriate to carry out the purposes of the Deposit Agreement and the applicable ADR(s), the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof. The manner in which a Beneficial Owner holds ADSs (e.g., in a brokerage account vs. as registered holder) may affect the rights and obligations of, the manner in which, and the extent to which, services are made available to, Beneficial Owners pursuant to the terms of the Deposit Agreement.

The statements made on the face and reverse of this ADR are summaries of certain provisions of the Deposit Agreement and the Articles of Association of the Company (as in effect on the date of the signing of the Deposit Agreement) and are qualified by and subject to the detailed provisions of the Deposit Agreement and the Articles of Association, to which reference is hereby made.

All capitalized terms not defined herein shall have the meanings ascribed thereto in the Deposit Agreement.

The Depositary makes no representation or warranty as to the validity or worth of the Deposited Property. The Depositary has made arrangements for the acceptance of the ADSs into DTC. Each Beneficial Owner of ADSs held through DTC must rely on the procedures of DTC and the DTC Participants to exercise and be entitled to any rights attributable to such ADSs. The Depositary may issue Uncertificated ADSs subject, however, to the terms and conditions of Section 2.13 of the Deposit Agreement.

(2) **Surrender of ADSs and Withdrawal of Deposited Securities.** The Holder of this ADR (and of the ADSs evidenced hereby) shall be entitled to Delivery (at the Custodian's designated office) of the Deposited Securities at the time represented by the ADSs evidenced hereby upon satisfaction of each of the following conditions: (i) the Holder (or a duly-authorized attorney of the Holder) has duly Delivered ADSs to the Depositary at its Principal Office the ADSs evidenced hereby (and, if applicable, this ADR evidencing such ADSs) for the purpose of withdrawal of the Deposited Securities represented thereby, (ii) if applicable and so required by the Depositary, this ADR Delivered to the Depositary for such purpose has been properly

endorsed in blank or is accompanied by proper instruments of transfer in blank (including signature guarantees in accordance with standard securities industry practice), (iii) if so required by the Depositary, the Holder of the ADSs has executed and delivered to the Depositary a written order directing the Depositary to cause the Deposited Securities being withdrawn to be Delivered to or upon the written order of the person(s) designated in such order, and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 of, and Exhibit B to, the Deposit Agreement) have been paid, *subject, however, in each case*, to the terms and conditions of this ADR evidencing the surrendered ADSs, of the Deposit Agreement, of the Company's Articles of Association and of any applicable laws and the rules of CREST, and to any provisions of or governing the Deposited Securities, in each case as in effect at the time thereof.

Upon satisfaction of each of the conditions specified above, the Depositary (i) shall cancel the ADSs Delivered to it (and, if applicable, this ADR(s) evidencing the ADSs so Delivered), (ii) shall direct the Registrar to record the cancellation of the ADSs so Delivered on the books maintained for such purpose, and (iii) shall direct the Custodian to Deliver, or cause the Delivery of, in each case, without unreasonable delay, the Deposited Securities represented by the ADSs so canceled together with any certificate or other document of title for the Deposited Securities, or evidence of the electronic transfer thereof (if available), as the case may be, to or upon the written order of the person(s) designated in the order delivered to the Depositary for such purpose, *subject however, in each case*, to the terms and conditions of the Deposit Agreement, of this ADR evidencing the ADS so canceled, of the Articles of Association of the Company, of any applicable laws and of the rules of CREST, and to the terms and conditions of or governing the Deposited Securities, in each case as in effect at the time thereof.

The Depositary shall not accept for surrender ADSs representing less than one (1) Share. In the case of Delivery to it of ADSs representing a number other than a whole number of Shares, the Depositary shall cause ownership of the appropriate whole number of Shares to be Delivered in accordance with the terms hereof, and shall, at the discretion of the Depositary, either (i) return to the person surrendering such ADSs the number of ADSs representing any remaining fractional Share, or (ii) sell or cause to be sold the fractional Share represented by the ADSs so surrendered and remit the proceeds of such sale (net of (a) applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes required to be withheld) to the person surrendering the ADSs.

Notwithstanding anything else contained in this ADR or the Deposit Agreement, the Depositary may make delivery at the Principal Office of the Depositary of Deposited Property consisting of (i) any cash dividends or cash distributions, or (ii) any proceeds from the sale of any non-cash distributions, which are at the time held by the Depositary in respect of the Deposited Securities represented by the ADSs surrendered for cancellation and withdrawal. At the request, risk and expense of any Holder so surrendering ADSs represented by this ADR, and for the account of such Holder, the Depositary shall direct the Custodian to forward (to the extent permitted by law) any Deposited Property (other than Deposited Securities) held by the Custodian in respect of such ADSs to the Depositary for delivery at the Principal Office of the Depositary. Such direction shall be given by letter or, at the request, risk and expense of such Holder, by cable, telex or facsimile transmission.

(3) Transfer, Combination and Split-up of ADRs. The Registrar shall register the transfer of this ADR (and of the ADSs represented hereby) on the books maintained for such purpose and the Depositary shall (x) cancel this ADR and execute new ADRs evidencing the same aggregate number of ADSs as those evidenced by this ADR canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs, and (z) Deliver such new ADRs to or upon the order of the person entitled thereto, if each of the following conditions has been satisfied: (i) this ADR has been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a transfer thereof, (ii) this surrendered ADR has been properly endorsed or is accompanied by proper instruments of transfer (including signature guarantees in accordance with standard securities industry practice), (iii) this surrendered ADR has been duly stamped (if required by the laws of the State of New York or of the United States), and (iv) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 of, and Exhibit B to, the Deposit Agreement) have been paid, *subject, however, in each case*, to the terms and conditions of this ADR, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.

The Registrar shall register the split-up or combination of this ADR (and of the ADSs represented hereby) on the books maintained for such purpose and the Depositary shall (x) cancel this ADR and execute new ADRs for the number of ADSs requested, but in the aggregate not exceeding the number of ADSs evidenced by this ADR canceled by the Depositary, (y) cause the Registrar to countersign such new ADRs, and (z) Deliver such new ADRs to or upon the order of the Holder thereof, if each of the following conditions has been satisfied: (i) this ADR has been duly Delivered by the Holder (or by a duly authorized attorney of the Holder) to the Depositary at its Principal Office for the purpose of effecting a split-up or combination hereof, and (ii) all applicable fees and charges of, and expenses incurred by, the Depositary and all applicable taxes and governmental charges (as are set forth in Section 5.9 of, and Exhibit B to, the Deposit Agreement) have been paid, *subject, however, in each case*, to the terms and conditions of this ADR, of the Deposit Agreement and of applicable law, in each case as in effect at the time thereof.

(4) Pre-Conditions to Registration, Transfer, Etc. As a condition precedent to the execution and Delivery, the registration of issuance, transfer, split-up, combination or surrender, of any ADS, the delivery of any distribution thereon, or the withdrawal of any Deposited Property, the Depositary or the Custodian may require (i) payment from the depositor of Shares or presenter of ADSs or of this ADR of a sum sufficient to reimburse it for any tax or other governmental charge and any stock transfer or registration fee with respect thereto (including any such tax or charge and fee with respect to Shares being deposited or withdrawn) and payment of any applicable fees and charges of the Depositary as provided in Section 5.9 and Exhibit B to the Deposit Agreement and in this ADR, (ii) the production of proof reasonably satisfactory to it as to the identity and genuineness of any signature or any other matter contemplated by Section 3.1 of the Deposit Agreement, and (iii) compliance with (A) any laws or governmental regulations relating to the execution and Delivery of this ADR or ADSs or to the withdrawal of Deposited Securities and (B) such reasonable regulations as the Depositary and the Company may establish consistent with the provisions of this ADR, if applicable, the Deposit Agreement and applicable law.

The issuance of ADSs against deposits of Shares generally or against deposits of particular Shares may be suspended, or the deposit of particular Shares may be refused, or the registration of transfer of ADSs in particular instances may be refused, or the registration of transfer of ADSs generally may be suspended, during any period when the transfer books of the Company, the Depositary, a Registrar or the Share Registrar are closed or if any such action is deemed necessary or advisable by the Depositary or the Company, in good faith, at any time or from time to time because of any requirement of law or regulation, any government or governmental body or commission or any securities exchange on which the ADSs or Shares are listed, or under any provision of the Deposit Agreement or this ADR, if applicable, or under any provision of, or governing, the Deposited Securities, or because of a meeting of shareholders of the Company or for any other reason, subject, in all cases to Section 7.8 (a) of the Deposit Agreement and paragraph (25) of this ADR. Notwithstanding any provision of the Deposit Agreement or this ADR to the contrary, Holders are entitled to surrender outstanding ADSs to withdraw the Deposited Securities associated therewith at any time subject only to (i) temporary delays caused by closing the transfer books of the Depositary or the Company or the deposit of Shares in connection with voting at a shareholders' meeting or the payment of dividends, (ii) the payment of fees, taxes and similar charges, (iii) compliance with any U.S. or foreign laws or governmental regulations relating to the ADSs or to the withdrawal of the Deposited Securities, and (iv) other circumstances specifically contemplated by Instruction I.A.(l) of the General Instructions to Form F-6 (as such General Instructions may be amended from time to time).

(5) **Compliance With Information Requests.** Notwithstanding any other provision of the Deposit Agreement or this ADR, each Holder and Beneficial Owner of the ADSs represented hereby agrees to comply with requests from the Company pursuant to applicable law, the rules and requirements of any stock exchange on which the Shares or ADSs are, or will be, registered, traded or listed, or the Articles of Association of the Company, which are made to provide information, *inter alia*, as to the capacity in which such Holder or Beneficial Owner owns ADSs (and the Shares represented by such ADSs, as the case may be) and regarding the identity of any other person(s) interested in such ADSs (and the Shares represented by such ADSs, as the case may be) and the nature of such interest and various other matters, whether or not they are Holders and/or Beneficial Owners at the time of such request. The Depositary agrees to use its reasonable efforts to forward, upon the request of the Company and at the Company's expense, any such request from the Company to the Holders and to forward to the Company, as promptly as practicable, any such responses to such requests received by the Depositary.

(6) **Ownership Restrictions.** Notwithstanding any other provision contained in this ADR or of the Deposit Agreement to the contrary, the Company may restrict transfers of the Shares where such transfer might result in ownership of Shares exceeding limits imposed by applicable law or the Articles of Association of the Company. The Company may also restrict, in such manner as it deems appropriate, transfers of the ADSs where such transfer may result in the total number of Shares represented by the ADSs owned by a single Holder or Beneficial Owner to exceed any such limits. The Company may, in its sole discretion but subject to applicable law, instruct the Depositary to take action with respect to the ownership interest of any Holder or Beneficial Owner in excess of the limits set forth in the preceding sentence, including but not limited to, the imposition of restrictions on the transfer of ADSs, the removal or limitation of voting rights or the mandatory sale or disposition on behalf of a Holder or

Beneficial Owner of the Shares represented by the ADSs held by such Holder or Beneficial Owner in excess of such limitations, if and to the extent such disposition is permitted by applicable law and the Articles of Association of the Company. Nothing herein or in the Deposit Agreement shall be interpreted as obligating the Depositary or the Company to ensure compliance with the ownership restrictions described herein or in Section 3.5 of the Deposit Agreement.

Notwithstanding any provision of the Deposit Agreement or of the ADRs and without limiting the foregoing, by being a Holder of an ADR, each such Holder agrees to provide such information as the Company may request in a disclosure notice (a "Disclosure Notice") given pursuant to the U.K. Companies Act 2006 (as amended from time to time and including any statutory modification or re-enactment thereof, the "Companies Act") or the Articles of Association of the Company. By accepting or holding an ADR, each Holder acknowledges that it understands that failure to comply with a Disclosure Notice may result in the imposition of sanctions against the holder of the Shares in respect of which the non-complying person is or was, or appears to be or has been, interested as provided in the Companies Act and the Articles of Association which currently include, the withdrawal of the voting rights of such Shares and the imposition of restrictions on the rights to receive dividends on and to transfer such Shares.

The Company reserves the right to instruct Holders to deliver their ADSs for cancellation and withdrawal of the Deposited Securities so as to permit the Company to deal directly with the Holder thereof as a holder of Shares and Holders agree to comply with such instructions. The Depositary agrees to cooperate with the Company in its efforts to inform Holders of the Company's exercise of its rights under this paragraph and agrees to consult with, and provide reasonable assistance without risk, liability or expense on the part of the Depositary, to the Company on the manner or manners in which it may enforce such rights with respect to any Holder.

(7) Reporting Obligations and Regulatory Approvals. Applicable laws and regulations may require holders and beneficial owners of Shares, including the Holders and Beneficial Owners of ADSs, to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. Holders and Beneficial Owners of ADSs are solely responsible for determining and complying with such reporting requirements and obtaining such approvals. Each Holder and each Beneficial Owner hereby agrees to make such determination, file such reports, and obtain such approvals to the extent and in the form required by applicable laws and regulations as in effect from time to time. Neither the Depositary, the Custodian, the Company or any of their respective agents or affiliates shall be required to take any actions whatsoever on behalf of Holders or Beneficial Owners to determine or satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

(8) Liability for Taxes and Other Charges. Any tax or other governmental charge payable by the Custodian or by the Depositary with respect to any Deposited Property, ADSs or this ADR shall be payable by the Holders and Beneficial Owners to the Depositary. The Company, the Custodian and/or the Depositary may withhold or deduct from any distributions made in respect of Deposited Property, and may sell for the account of a Holder and/or Beneficial Owner any or all of the Deposited Property and apply such distributions and sale proceeds in payment of, any taxes (including applicable interest and penalties) or charges that are

or may be payable by Holders or Beneficial Owners in respect of the ADSs, Deposited Property and this ADR, the Holder and the Beneficial Owner hereof remaining liable for any deficiency. The Custodian may refuse the deposit of Shares and the Depositary may refuse to issue ADSs, to deliver ADRs, register the transfer of ADSs, register the split-up or combination of ADRs and (subject to paragraph (25) of this ADR and Section 7.8(a) of the Deposit Agreement) the withdrawal of Deposited Property until payment in full of such tax, charge, penalty or interest is received. Every Holder and Beneficial Owner agrees to indemnify the Depositary, the Company, the Custodian, and any of their agents, officers, employees and Affiliates for, and to hold each of them harmless from, any claims with respect to taxes (including applicable interest and penalties thereon) arising from any tax benefit obtained for such Holder and/or Beneficial Owner. The obligations of Holders and Beneficial Owners under Section 3.2 of the Deposit Agreement shall survive any transfer of ADSs, any cancellation of ADSs and withdrawal of Deposited Securities, and the termination of the Deposit Agreement.

(9) **Representations and Warranties on Deposit of Shares.** Each person depositing Shares under the Deposit Agreement shall be deemed thereby to represent and warrant that (i) such Shares and the certificates therefor are duly authorized, validly allotted and issued, fully paid, not subject to any call for the payment of further capital and legally obtained by such person, (ii) all preemptive (and similar) rights, if any, with respect to such Shares have been validly waived, disapplied or exercised, (iii) the person making such deposit is duly authorized so to do, (iv) the Shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, (v) the Shares presented for deposit are not, and the ADSs issuable upon such deposit will not be, Restricted Securities (except as contemplated in Section 2.14 of the Deposit Agreement), and (vi) the Shares presented for deposit have not been stripped of any rights or entitlements and (vii) the deposit of the Shares does not violate any applicable provisions of English law. Such representations and warranties shall survive the deposit and withdrawal of Shares, the issuance and cancellation of ADSs in respect thereof and the transfer of such ADSs. If any such representations or warranties are false in any way, the Company and the Depositary shall be authorized, at the cost and expense of the person depositing Shares, to take any and all actions necessary to correct the consequences thereof.

(10) **Proofs, Certificates and Other Information.** Any person presenting Shares for deposit, any Holder and any Beneficial Owner may be required, and every Holder and Beneficial Owner agrees, from time to time to provide to the Depositary and the Custodian such proof of citizenship or residence, taxpayer status, payment of all applicable taxes or other governmental charges, exchange control approval, legal or beneficial ownership of ADSs and Deposited Property, compliance with applicable laws, the terms of the Deposit Agreement or this ADR evidencing the ADSs and the provisions of, or governing, the Deposited Property, to execute such certifications and to make such representations and warranties, and to provide such other information and documentation (or, in the case of Shares in registered form presented for deposit, such information relating to the registration on the books of the Company or of the Share Registrar) as the Depositary or the Custodian may deem necessary or proper or as the Company may reasonably require by written request to the Depositary consistent with its obligations under the Deposit Agreement and this ADR. The Depositary and the Registrar, as applicable, may withhold the execution or delivery or registration of transfer of any ADR or ADS or the distribution or sale of any dividend or distribution of rights or of the proceeds thereof

or, to the extent not limited by paragraph (25) and Section 7.8 (a) of the Deposit Agreement, the delivery of any Deposited Property until such proof or other information is filed or such certifications are executed, or such representations and warranties are made or such other documentation or information are provided, in each case to the Depositary's, the Registrar's and the Company's satisfaction. The Depositary shall provide the Company, in a timely manner, with copies or originals if necessary and appropriate of (i) any such proofs of citizenship or residence, taxpayer status, or exchange control approval or copies of written representations and warranties which it receives from Holders and Beneficial Owners, and (ii) any other information or documents which the Company may reasonably request and which the Depositary shall request and receive from any Holder or Beneficial Owner or any person presenting Shares for deposit or ADSs for cancellation, transfer or withdrawal. Nothing herein shall obligate the Depositary to (i) obtain any information for the Company if not provided by the Holders or Beneficial Owners, or (ii) verify or vouch for the accuracy of the information so provided by the Holders or Beneficial Owners.

(11) **ADS Fees and Charges.** The following ADS fees are payable under the terms of the Deposit Agreement:

(i) ADS Issuance Fee: by any person for whom ADSs are issued (*e.g.*, an issuance upon a deposit of Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason), excluding issuances as a result of distributions described in paragraph (iv) below, a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) issued under the terms of the Deposit Agreement;

(ii) ADS Cancellation Fee: by any person for whom ADSs are being cancelled (*e.g.*, a cancellation of ADSs for Delivery of deposited Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason), a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) cancelled;

(iii) Cash Distribution Fee: by any Holder of ADSs, a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) held for the distribution of cash dividends or other cash distributions (*e.g.*, upon a sale of rights and other entitlements);

(iv) Stock Distribution /Rights Exercise Fee: by any Holder of ADS(s), a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) held for the distribution of ADSs pursuant to (a) stock dividends or other free stock distributions, or (b) an exercise of rights to purchase additional ADSs;

(v) Other Distribution Fee: by any Holder of ADS(s), a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) held for the distribution of securities other than ADSs or rights to purchase additional ADSs (*e.g.*, spin-off shares);

(vi) Depositary Services Fee: by any Holder of ADS(s), a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the Depositary;

(vii) Registration of ADS Transfer Fee: by any Holder of ADS(s) being transferred or by any person to whom ADSs are transferred, a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) transferred (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and *vice versa*, or for any other reason); and

(viii) ADS Conversion Fee: by any Holder of ADS(s) being converted or by any person to whom the converted ADSs are delivered, a fee not in excess of U.S. $5.00 per 100 ADSs (or fraction thereof) converted from one ADS series to another ADS series (*e.g.*, upon conversion of Partial Entitlement ADSs for Full Entitlement ADSs, or upon conversion of Restricted ADSs into freely transferrable ADSs, and *vice versa*).

The Company, Holders, Beneficial Owners, persons depositing Shares or withdrawing Deposited Securities in connection with ADS issuances and cancellations, and persons for whom ADSs are issued or cancelled shall be responsible for the following ADS charges under the terms of the Deposit Agreement:

(a) taxes (including applicable interest and penalties) and other governmental charges;

(b) such registration fees as may from time to time be in effect for the registration of Shares or other Deposited Securities on the share register and applicable to transfers of Shares or other Deposited Securities to or from the name of the Custodian, the Depositary or any nominees upon the making of deposits and withdrawals, respectively;

(c) such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the Deposit Agreement to be at the expense of the person depositing Shares or withdrawing Deposited Property or of the Holders and Beneficial Owners of ADSs;

(d) in connection with the conversion of Foreign Currency, the fees, expenses, spreads, taxes and other charges of the Depositary and/or conversion service providers (which may be a division, branch or Affiliate of the Depositary). Such fees, expenses, spreads, taxes and other charges shall be deducted from the Foreign Currency;

(e) any reasonable and customary out-of-pocket expenses incurred in such conversion and/or on behalf of the Holders and Beneficial Owners in complying with currency exchange control or other governmental requirements; and

(f) the fees, charges, costs and expenses incurred by the Depositary, the Custodian, or any nominee in connection with the ADR program.

All ADS fees and charges so payable may be deducted from distributions or must be remitted to the Depositary, or its designee, and may, at any time and from time to time, be changed by agreement between the Depositary and Company but, in the case of ADS fees and charges payable by Holders and Beneficial Owners, only in the manner contemplated by paragraph (23) of this ADR and as contemplated in Section 6.1 of the Deposit Agreement. The Depositary shall provide, without charge, a copy of its latest ADS fee schedule to anyone upon request.

ADS fees and charges for (i) the issuance of ADSs and (ii) the cancellation of ADSs will be payable by the person for whom the ADSs are so issued by the Depositary (in the case of ADS issuances) and by the person for whom ADSs are being cancelled (in the case of ADS cancellations). In the case of ADSs issued by the Depositary into DTC or presented to the Depositary via DTC, the ADS issuance and cancellation fees and charges will be payable by the DTC Participant(s) receiving the ADSs from the Depositary or the DTC Participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the Beneficial Owner(s) and will be charged by the DTC Participant(s) to the account(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC Participant(s) as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are payable by Holders as of the applicable ADS Record Date established by the Depositary. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, the applicable Holders as of the ADS Record Date established by the Depositary will be invoiced for the amount of the ADS fees and charges and such ADS fees may be deducted from distributions made to Holders. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC Participants in accordance with the procedures and practices prescribed by DTC from time to time and the DTC Participants in turn charge the amount of such ADS fees and charges to the Beneficial Owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the ADS Holder whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the Holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to the Deposit Agreement, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges, and reimburse the Depositary for such out-of-pocket expenses, as the Depositary and the Company may agree from time to time. Responsibility for payment of such fees, charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such fees, charges and reimbursements to

the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary.

The obligations of Holders and Beneficial Owners to pay ADS fees and charges shall survive the termination of the Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in Section 5.4 of the Deposit Agreement, the right to collect ADS fees and charges shall extend for those ADS fees and charges incurred prior to the effectiveness of such resignation or removal.

(12) Title to ADRs. Subject to the limitations contained in the Deposit Agreement and in this ADR, it is a condition of this ADR, and every successive Holder of this ADR by accepting or holding the same consents and agrees, that title to this ADR (and to each Certificated ADS evidenced hereby) shall be transferable upon the same terms as a certificated security under the laws of the State of New York, provided that, in the case of Certificated ADSs, this ADR has been properly endorsed or is accompanied by proper instruments of transfer. Notwithstanding any notice to the contrary, the Depositary and the Company may deem and treat the Holder of this ADR (that is, the person in whose name this ADR is registered on the books of the Depositary) as the absolute owner thereof for all purposes. Neither the Depositary nor the Company shall have any obligation nor be subject to any liability under the Deposit Agreement or this ADR to any holder of this ADR or any Beneficial Owner unless, in the case of a holder of ADSs, such holder is the Holder of this ADR registered on the books of the Depositary or, in the case of a Beneficial Owner, such Beneficial Owner, or the Beneficial Owner's representative, is the Holder registered on the books of the Depositary.

(13) Validity of ADR. The Holder(s) of this ADR (and the ADSs represented hereby) shall not be entitled to any benefits under the Deposit Agreement or be valid or enforceable for any purpose against the Depositary or the Company unless this ADR has been (i) dated, (ii) signed by the manual or facsimile signature of a duly-authorized signatory of the Depositary, (iii) countersigned by the manual or facsimile signature of a duly-authorized signatory of the Registrar, and (iv) registered in the books maintained by the Registrar for the registration of issuances and transfers of ADRs. An ADR bearing the facsimile signature of a duly-authorized signatory of the Depositary or the Registrar, who at the time of signature was a duly authorized signatory of the Depositary or the Registrar, as the case may be, shall bind the Depositary, notwithstanding the fact that such signatory has ceased to be so authorized prior to the delivery of such ADR by the Depositary.

(14) Available Information; Reports; Inspection of Transfer Books.

The Company is subject to the periodic reporting requirements of the Exchange Act and, accordingly, is required to file or furnish certain reports with the Commission. These reports can be retrieved from the Commission's website (www.sec.gov) and can be inspected and copied at the public reference facilities maintained by the Commission located (as of the date of the Deposit Agreement) at 100 F Street, N.E., Washington D.C. 20549. The Depositary shall make available for inspection by Holders at its Principal Office, as promptly as practicable after receipt thereof, any reports and communications, including any proxy soliciting materials, received from the Company which are both (a) received by the Depositary, the Custodian, or the nominee of either of them as the holder of the Deposited Property and (b) made generally available to the

holders of such Deposited Property by the Company. The Depositary shall also provide or make available to Holders copies of such reports when furnished by the Company pursuant to Section 5.6 of the Deposit Agreement.

The Registrar shall keep books for the registration of ADSs which at all reasonable times shall be open for inspection by the Company and by the Holders of such ADSs, provided that such inspection shall not be, to the Registrar's knowledge, for the purpose of communicating with Holders of such ADSs in the interest of a business or object other than the business of the Company or other than a matter related to the Deposit Agreement or the ADSs.

The Registrar may close the transfer books with respect to the ADSs, at any time or from time to time, when deemed necessary or advisable by it in good faith in connection with the performance of its duties hereunder, or at the reasonable written request of the Company subject, in all cases, to paragraph (25) and Section 7.8 (a) of the Deposit Agreement.

Dated:

CITIBANK, N.A.
Transfer Agent and Registrar

By: _____
Authorized Signatory

CITIBANK, N.A.
as Depositary

By: _____
Authorized Signatory

The address of the Principal Office of the Depositary is 388 Greenwich Street, New York, New York 10013, U.S.A.

[FORM OF REVERSE OF ADR]

SUMMARY OF CERTAIN ADDITIONAL PROVISIONS

OF THE DEPOSIT AGREEMENT

(15) Dividends and Distributions in Cash, Shares, etc. (a) ***Cash Distributions***: Upon the timely receipt by the Depositary of a notice from the Company that it intends to make a distribution of a cash dividend or other cash distribution, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9 of the Deposit Agreement. Upon receipt of confirmation of receipt of (x) any cash dividend or other cash distribution on any Deposited Securities, or (y) proceeds from the sale of any Deposited Property held in respect of the ADSs under the terms of the Deposit Agreement, the Depositary will (i) if at the time of receipt thereof any amounts received in a Foreign Currency can, in the judgment of the Depositary (pursuant to Section 4.8 of the Deposit Agreement), be converted on a practicable basis into Dollars transferable to the United States, promptly convert or cause to be converted such cash dividend, distribution or proceeds into Dollars (subject to the terms and conditions described in Section 4.8 of the Deposit Agreement), (ii) if applicable and unless previously established, establish the ADS Record Date upon the terms described in Section 4.9 of the Deposit Agreement, and (iii) distribute promptly the amount thus received from such conversion (net of (a) the applicable fees and charges described in the Fee Schedule attached as Exhibit B to the Deposit Agreement and (b) applicable taxes required to be withheld in connection with the distribution) to the Holders entitled thereto as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date. The Depositary shall distribute only such amount, however, as can be distributed without attributing to any Holder a fraction of one cent, and any balance not so distributed shall be held by the Depositary (without liability for interest thereon) and shall be added to and become part of the next sum received by the Depositary for distribution to Holders of ADSs outstanding at the time of the next distribution. If the Company, the Custodian or the Depositary is required to withhold and does withhold from any cash dividend or other cash distribution in respect of any Deposited Securities, or from any cash proceeds from the sales of Deposited Property, an amount on account of taxes, duties or other governmental charges, the amount distributed to Holders on the ADSs shall be reduced accordingly. Such withheld amounts shall be forwarded by the Company, the Custodian or the Depositary to the relevant governmental authority. Evidence of payment thereof by the Company shall be forwarded by the Company to the Depositary upon request. The Depositary will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable Holders and Beneficial Owners of ADSs until the distribution can be effected or the funds that the Depositary holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for above, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.1 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.1 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(b) ***Share Distributions***: Upon the timely receipt by the Depositary of a notice from the Company that it intends to make a distribution that consists of a dividend in, or free distribution of Shares, the Depositary shall establish the ADS Record Date upon the terms described in Section 4.9 of the Deposit Agreement. Upon receipt of confirmation from the Custodian of the receipt of the Shares so distributed by the Company, the Depositary shall either (i) subject to Section 5.9 of the Deposit Agreement, distribute to the Holders as of the ADS Record Date in proportion to the number of ADSs held as of the ADS Record Date, additional ADSs, which represent in the aggregate the number of Shares received as such dividend, or free distribution, subject to the other terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary and (b) applicable taxes to be withheld), or (ii) if additional ADSs are not so distributed, take all actions necessary so that each ADS issued and outstanding after the ADS Record Date shall, to the extent permissible by law, thenceforth also represent rights and interests in the additional integral number of Shares distributed upon the Deposited Securities represented thereby (net of (a) the applicable fees and charges of, and expenses incurred by, the Depositary, and (b) applicable taxes). In lieu of delivering fractional ADSs, the Depositary shall sell the number of Shares or ADSs, as the case may be, represented by the aggregate of such fractions and distribute the net proceeds upon the terms described in Section 4.1 of the Deposit Agreement.

In the event that the Depositary determines that any distribution in property (including Shares) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, or, if the Company in the fulfillment of its obligations under Section 5.7 of the Deposit Agreement, has furnished an opinion of U.S. counsel determining that Shares must be registered under the Securities Act or other laws in order to be distributed to Holders (and no such registration statement has been declared effective), the Depositary may dispose of all or a portion of such property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable, and the Depositary shall distribute the net proceeds of any such sale (after deduction of (a) applicable taxes required to be withheld and (b) fees and charges of, and the expenses incurred by, the Depositary) to Holders entitled thereto upon the terms of Section 4.1 of the Deposit Agreement. The Depositary shall hold and/or distribute any unsold balance of such property in accordance with the provisions of the Deposit Agreement. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for above, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.2 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.2 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(c) ***Elective Distributions in Cash or Shares***: Upon the timely receipt of a notice indicating that the Company wishes an elective distribution in cash or Shares to be made available to Holders of ADSs upon the terms described in the Deposit Agreement, the Company and the Depositary shall determine in accordance with the Deposit Agreement whether such distribution is lawful and reasonably practicable. The Depositary shall make such elective distribution available to Holders only if (i) the Company shall have timely requested that the elective distribution be made available to Holders, (ii) the Depositary shall have determined that

such distribution is reasonably practicable and (iii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement. If the above conditions are satisfied, the Depositary shall, subject to the terms and conditions of the Deposit Agreement, establish the ADS Record Date according to paragraph (16) and Section 4.9 of the Deposit Agreement and establish procedures to enable the Holder hereof to elect to receive the proposed distribution in cash or in additional ADSs. If a Holder elects to receive the distribution in cash, the distribution shall be made as in the case of a distribution in cash. If the Holder hereof elects to receive the distribution in additional ADSs, the distribution shall be made as in the case of a distribution in Shares upon the terms described in the Deposit Agreement. If such elective distribution is not reasonably practicable or if the Depositary did not receive satisfactory documentation set forth in the Deposit Agreement, the Depositary shall establish an ADS Record Date upon the terms of Section 4.9 of the Deposit Agreement and, to the extent permitted by law, distribute to Holders, on the basis of the same determination as is made in England and Wales in respect of the Shares for which no election is made, either (x) cash upon the terms described in Section 4.1 of the Deposit Agreement or (y) additional ADSs representing such additional Shares, in each case, upon the terms described in Section 4.2 of the Deposit Agreement. Nothing herein or in the Deposit Agreement shall obligate the Depositary to make available to the Holder hereof a method to receive the elective distribution in Shares (rather than ADSs). There can be no assurance that the Holder hereof or Holders generally will be given the opportunity to receive elective distributions on the same terms and conditions as the holders of Shares. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed distribution provided for above, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.3 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.3 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(d) ***Distribution of Rights to Purchase Additional ADSs***: Upon the timely receipt by the Depositary of a notice indicating that the Company wishes rights to subscribe for additional Shares to be made available to Holders of ADSs, the Depositary upon consultation with the Company, shall determine, whether it is lawful and reasonably practicable to make such rights available to the Holders. The Depositary shall make such rights available to any Holders only if (i) the Company shall have timely requested that such rights be made available to Holders, (ii) the Depositary shall have received satisfactory documentation within the terms of Section 5.7 of the Deposit Agreement, and (iii) the Depositary shall have determined that such distribution of rights is reasonably practicable. If such conditions are not satisfied or if the Company requests that the rights not be made available to Holders of ADSs, the Depositary shall proceed with the sale of the rights as described below. In the event all conditions set forth above are satisfied, the Depositary shall establish the ADS Record Date (upon the terms described in Section 4.9 of the Deposit Agreement) and establish procedures to (x) distribute rights to purchase additional ADSs (by means of warrants or otherwise), (y) enable the Holders to exercise such rights (upon payment of the subscription price and of the applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes), and (z) deliver ADSs upon the valid exercise of such rights. The Company shall assist the Depositary to the extent necessary in establishing such procedures. Nothing herein or in the Deposit Agreement shall obligate the Depositary to make

available to the Holders a method to exercise rights to subscribe for Shares (rather than ADSs). If (i) the Company does not timely request the Depositary to make the rights available to Holders or requests that the rights not be made available to Holders, (ii) the Depositary fails to receive satisfactory documentation within the terms of Section 5,7 of the Deposit Agreement or determines it is not reasonably practicable to make the rights available to Holders, or (iii) any rights made available are not exercised and appear to be about to lapse, the Depositary shall determine whether it is lawful and reasonably practicable to sell such rights, in a riskless principal capacity, at such place and upon such terms (including public and private sale) as it may deem practicable. The Depositary shall, upon such sale, convert and distribute proceeds of such sale (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) upon the terms hereof and of Section 4.1 of the Deposit Agreement. If the Depositary is unable to make any rights available to Holders upon the terms described in Section 4.4(a) of the Deposit Agreement or to arrange for the sale of the rights upon the terms described in Section 4.4(b) of the Deposit Agreement, the Depositary shall allow such rights to lapse. The Depositary shall not be liable for (i) any failure to accurately determine whether it may be lawful or practicable to make such rights available to Holders in general or any Holders in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale or exercise, or (iii) the content of any materials forwarded to the Holders on behalf of the Company in connection with the rights distribution.

Notwithstanding anything herein or in Section 4.4 of the Deposit Agreement to the contrary, if registration (under the Securities Act or any other applicable law) of the rights or the securities to which any rights relate may be required in order for the Company to offer such rights or such securities to Holders and to sell the securities represented by such rights, the Depositary will not distribute such rights to the Holders (i) unless and until a registration statement under the Securities Act (or other applicable law) covering such offering is in effect or (ii) unless the Company furnishes the Depositary opinion(s) of counsel for the Company in the United States and counsel to the Company in any other applicable country in which rights would be distributed, in each case satisfactory to the Depositary, to the effect that the offering and sale of such securities to Holders and Beneficial Owners are exempt from, or do not require registration under, the provisions of the Securities Act or any other applicable laws. In the event that the Company, the Depositary or the Custodian shall be required to withhold and does withhold from any distribution of Deposited Property (including rights) an amount on account of taxes or other governmental charges, the amount distributed to the Holders of ADSs shall be reduced accordingly. In the event that the Depositary determines that any distribution of Deposited Property (including Shares and rights to subscribe therefor) is subject to any tax or other governmental charges which the Depositary is obligated to withhold, the Depositary may dispose of all or a portion of such Deposited Property (including Shares and rights to subscribe therefor) in such amounts and in such manner, including by public or private sale, as the Depositary deems necessary and practicable to pay any such taxes or charges.

There can be no assurance that Holders generally, or any Holder in particular, will be given the opportunity to receive or exercise rights on the same terms and conditions as the holders of Shares or be able to exercise such rights. Nothing herein or in the Deposit Agreement shall obligate the Company to file any registration statement in respect of any rights or Shares or other securities to be acquired upon the exercise of such rights.

(e) ***Distributions other than Cash, Shares or Rights to Purchase Shares***: Upon receipt of a notice indicating that the Company wishes property other than cash, Shares or rights to purchase additional Shares to be made to Holders of ADSs, the Depositary shall determine whether such distribution to Holders is lawful and reasonably practicable. The Depositary shall not make such distribution unless (i) the Company shall have requested the Depositary to make such distribution to Holders, (ii) the Depositary shall have received satisfactory documentation contemplated in Section 5.7 of the Deposit Agreement, and (iii) the Depositary shall have determined that such distribution is reasonably practicable. Upon satisfaction of such conditions, the Depositary shall distribute the property so received to the Holders of record, as of the ADS Record Date, in proportion to the number of ADSs held by them respectively and in such manner as the Depositary may deem practicable for accomplishing such distribution (i) upon receipt of payment or net of the applicable fees and charges of, and expenses incurred by, the Depositary, and (ii) net of any applicable taxes required to be withheld. The Depositary may dispose of all or a portion of the property so distributed and deposited, in such amounts and in such manner (including public or private sale) as the Depositary may deem practicable or necessary to satisfy any taxes (including applicable interest and penalties) or other governmental charges applicable to the distribution.

If the conditions above are not satisfied, the Depositary shall sell or cause such property to be sold in a public or private sale, at such place or places and upon such terms as it may deem practicable and shall (i) cause the proceeds of such sale, if any, to be converted into Dollars and (ii) distribute the proceeds of such conversion received by the Depositary (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) to the Holders as of the ADS Record Date upon the terms hereof and of Section 4.1 of the Deposit Agreement. If the Depositary is unable to sell such property, the Depositary may dispose of such property for the account of the Holders in any way it deems reasonably practicable under the circumstances.

Neither the Depositary nor the Company shall be responsible for (i) any failure to determine whether it is lawful or practicable to make the property described in Section 4.5 of the Deposit Agreement available to Holders in general or any Holders in particular, nor (ii) any loss incurred in connection with the sale or disposal of such property.

(16) Redemption. Upon timely receipt of notice from the Company that it intends to exercise its right of redemption in respect of any of the Deposited Securities, and satisfactory documentation, and upon determining that such proposed redemption is practicable, the Depositary shall (to the extent practicable) provide to each Holder a notice setting forth the Company's intention to exercise the redemption rights and any other particulars set forth in the Company's notice to the Depositary. The Depositary shall instruct the Custodian to present to the Company the Deposited Securities in respect of which redemption rights are being exercised against payment of the applicable redemption price. Upon receipt of confirmation from the Custodian that the redemption has taken place and that funds representing the redemption price have been received, the Depositary shall convert, transfer, and distribute the proceeds (net of applicable (a) fees and charges of, and the expenses incurred by, the Depositary, and (b) taxes), retire ADSs and cancel ADRs, if applicable, upon delivery of such ADSs by Holders thereof and the terms set forth in Sections 4.1 and 6.2 of the Deposit Agreement. If less than all outstanding Deposited Securities are redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as may be determined by the Depositary after consultation with the Company. The

redemption price per ADS shall be the dollar equivalent of the per share amount received by the Depositary (adjusted to reflect the ADS(s)-to-Share(s) ratio) upon the redemption of the Deposited Securities represented by ADSs (subject to the terms of Section 4.8 of the Deposit Agreement and the applicable fees and charges of, and expenses incurred by, the Depositary, and applicable taxes) multiplied by the number of Deposited Securities represented by each ADS redeemed. Notwithstanding anything contained in the Deposit Agreement to the contrary, in the event the Company fails to give the Depositary timely notice of the proposed redemption provided for above, the Depositary agrees to use commercially reasonable efforts to perform the actions contemplated in Section 4.7 of the Deposit Agreement, and the Company, the Holders and the Beneficial Owners acknowledge that the Depositary shall have no liability for the Depositary's failure to perform the actions contemplated in Section 4.7 of the Deposit Agreement where such notice has not been so timely given, other than its failure to use commercially reasonable efforts, as provided herein.

(17) **Fixing of ADS Record Date.** Whenever (a) the Depositary shall receive notice of the fixing of a record date by the Company for the determination of holders of Deposited Securities entitled to receive any distribution (whether in cash, Shares, rights or other distribution), (b) for any reason the Depositary causes a change in the number of Shares that are represented by each ADS, (c) the Depositary shall receive notice of any meeting of, or solicitation of consents or proxies of, holders of Shares or other Deposited Securities, or (d) the Depositary shall find it necessary or convenient in connection with the giving of any notice, solicitation of any consent or any other matter, the Depositary shall fix the record date (the "ADS Record Date") for the determination of the Holders of ADS(s) who shall be entitled to receive such distribution, to give instructions for the exercise of voting rights at any such meeting, to give or withhold such consent, to receive such notice or solicitation or to otherwise take action, or to exercise the rights of Holders with respect to such changed number of Shares represented by each ADS. The Depositary shall make reasonable efforts to establish the ADS Record Date as closely as practicable to the applicable record date for the Deposited Securities (if any) set by the Company in England and Wales and shall not announce the establishment of any ADS Record Date prior to the relevant corporate action having been made public by the Company (if such corporate action affects the Deposited Securities). Subject to applicable law, the terms and conditions of this ADR and Sections 4.1 through 4.8 of the Deposit Agreement, only the Holders of ADSs at the close of business in New York on such ADS Record Date shall be entitled to receive such distribution, to give such voting instructions, to receive such notice or solicitation, or otherwise take action.

(18) **Voting of Deposited Securities.** As soon as practicable after receipt of notice of any meeting at which the holders of Deposited Securities are entitled to vote, or of solicitation of consents or proxies from holders of Deposited Securities, the Depositary shall fix the ADS Record Date in respect of such meeting or solicitation of consent or proxy in accordance with Section 4.9 of the Deposit Agreement. The Depositary shall, if requested by the Company in writing in a timely manner (the Depositary having no obligation to take any further action if the request shall not have been received by the Depositary at least thirty (30) days prior to the date of such vote or meeting), at the Company's expense and provided no U.S. legal prohibitions exist, distribute as soon as practicable after receipt thereof to Holders as of the ADS Record Date: (a) such notice of meeting or solicitation of consent or proxy, (b) a statement that the Holders at the close of business on the ADS Record Date will be entitled, subject to any applicable law, the

provisions of the Deposit Agreement, the Articles of Association of the Company and the provisions of or governing the Deposited Securities (which provisions, if any, shall be summarized in pertinent part by the Company), to instruct the Depositary as to the exercise of the voting rights, if any, pertaining to the Deposited Securities represented by such Holder's ADSs, and (c) a brief statement as to the manner and timing (such timing to be determined after consultation with the Company) in which such voting instructions may be given to the Depositary or in which voting instructions may be deemed to have been given in accordance with Section 4.10 of the Deposit Agreement if no instructions are received prior to the deadline set for such purposes to the Depositary to give a discretionary proxy to a person designated by the Company.

Notwithstanding anything contained in the Deposit Agreement or any ADR, with the Company's prior written consent, the Depositary may, to the extent not prohibited by law or regulations, or by the requirements of the stock exchange on which the ADSs may be listed, in lieu of distribution of the materials provided to the Depositary in connection with any meeting of, or solicitation of consents or proxies from, holders of Deposited Securities, distribute to the Holders a notice that provides Holders with, or otherwise publicizes to Holders, instructions on how to retrieve such materials or receive such materials upon request (*e.g.*, by reference to a website containing the materials for retrieval or a contact for requesting copies of the materials).

The Depositary has been advised by the Company that the Articles of Association (as in effect on the date hereof), provide that voting at any meeting of shareholders is by show of hands unless a poll is demanded. The Depositary will not join in demanding a poll, whether or not requested to do so by Holders of ADSs. Under the Articles of Association (as in effect on the date hereof) a poll may be demanded by (i) the chairman of the meeting; (ii) by at least two members of the Company present in person (or by proxy), in each case, for the time being entitled to vote at the meeting; (iii) by any member or members of the Company present in person (or by proxy), in each case, for the time being entitled to vote at the meeting representing at least one-tenth of the total voting rights of all the members having the right to vote at the meeting; or (iv) by any member or members of the Company present in person (or by proxy), in each case, holding shares conferring a right to vote at the meeting, being shares on which an aggregate sum has been paid up equal to at least one-tenth of the total sum paid up on all the shares conferring that right.

Voting instructions may be given only in respect of a number of ADSs representing an integral number of Deposited Securities. Upon the timely receipt from a Holder of ADSs as of the ADS Record Date of voting instructions in the manner specified by the Depositary, the Depositary shall endeavor, insofar as practicable and permitted under any applicable law, the provisions of the Deposit Agreement, the Articles of Association of the Company and the provisions of the Deposited Securities, to vote, or cause the Custodian to vote, the Deposited Securities (in person or by proxy) represented by such Holder's ADSs as follows: (i) in the event voting takes place at a shareholders' meeting by a show of hands, the Depositary will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided voting instructions, and (ii) in the event voting takes place at a shareholders' meeting by poll, the Depositary will instruct the Custodian to vote the Deposited Securities in accordance with the voting instructions received from the Holders of ADSs. If voting is by poll and the Depositary does not receive voting instructions

from a Holder as of the ADS Record Date on or before the date established by the Depositary for such purpose, such Holder shall be deemed, and the Depositary shall deem such Holder, to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities; provided, however, that no such discretionary proxy shall be given by the Depositary with respect to any matter to be voted upon as to which the Company informs the Depositary that (a) the Company does not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of Deposited Securities may be adversely affected.

Deposited Securities represented by ADSs for which no timely voting instructions are received by the Depositary from the Holder shall not be voted (except (a) in the case voting is by show of hands, in which case the Depositary will instruct the Custodian to vote all Deposited Securities in accordance with the voting instructions received from a majority of Holders of ADSs who provided timely voting instructions, and (b) as contemplated in Section 4.10 of the Deposit Agreement). Neither the Depositary nor the Custodian shall under any circumstances exercise any discretion as to voting and neither the Depositary nor the Custodian shall vote, attempt to exercise the right to vote, or in any way make use of, for purposes of establishing a quorum or otherwise, the Deposited Securities represented by ADSs, except pursuant to and in accordance with the voting instructions timely received from Holders or as otherwise contemplated herein. If the Depositary timely receives voting instructions from a Holder which fail to specify the manner in which the Depositary is to vote the Deposited Securities represented by such Holder's ADSs, the Depositary will deem such Holder (unless otherwise specified in the notice distributed to Holders) to have instructed the Depositary to vote in favor of the items set forth in such voting instructions.

Notwithstanding anything else contained herein, the Depositary shall, if so requested in writing by the Company, represent all Deposited Securities (whether or not voting instructions have been received in respect of such Deposited Securities from Holders as of the ADS Record Date) for the sole purpose of establishing quorum at a meeting of shareholders.

Notwithstanding anything else contained in the Deposit Agreement or any ADR, the Depositary shall not have any obligation to take any action with respect to any meeting, or solicitation of consents or proxies, of holders of Deposited Securities if the taking of such action would violate U.S. or English laws. The Company agrees to take any and all actions reasonably necessary and as permitted by the laws of England and Wales to enable Holders and Beneficial Owners to exercise the voting rights accruing to the Deposited Securities and to deliver to the Depositary an opinion of U.S. counsel addressing any actions requested to be taken if so requested by the Depositary.

There can be no assurance that Holders generally or any Holder in particular will receive the notice described above with sufficient time to enable the Holder to return voting instructions to the Depositary in a timely manner.

(19) Changes Affecting Deposited Securities. Upon any change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of Deposited Securities, or upon any recapitalization, reorganization, merger, consolidation or sale of assets affecting the Company or to which it is a party, any property which shall be received by the Depositary or the Custodian in exchange for, or in conversion of, or replacement of, or otherwise in respect of,

such Deposited Securities shall, to the extent permitted by law, be treated as new Deposited Property under the Deposit Agreement, and this ADR shall, subject to the provisions of the Deposit Agreement, this ADR evidencing such ADSs and applicable law, represent the right to receive such additional or replacement Deposited Property. In giving effect to such change, split-up, cancellation, consolidation or other reclassification of Deposited Securities, recapitalization, reorganization, merger, consolidation or sale of assets, the Depositary may, with the Company's approval, and shall, if the Company shall so request, subject to the terms of the Deposit Agreement (including, without limitation, (a) the applicable fees and charges of, and expenses incurred by, the Depositary, and (b) applicable taxes) and receipt of an opinion of counsel to the Company satisfactory to the Depositary that such actions are not in violation of any applicable laws or regulations, (i) issue and deliver additional ADSs as in the case of a stock dividend on the Shares, (ii) amend the Deposit Agreement and the applicable ADRs, (iii) amend the applicable Registration Statement(s) on Form F-6 as filed with the Commission in respect of the ADSs, (iv) call for the surrender of outstanding ADRs to be exchanged for new ADRs, and (v) take such other actions as are appropriate to reflect the transaction with respect to the ADSs. The Company agrees to, jointly with the Depositary, amend the Registration Statement on Form F-6 as filed with the Commission to permit the issuance of such new form of ADRs. Notwithstanding the foregoing, in the event that any Deposited Property so received may not be lawfully distributed to some or all Holders, the Depositary may, with the Company's approval, and shall, if the Company requests, subject to receipt of an opinion of Company's counsel satisfactory to the Depositary that such action is not in violation of any applicable laws or regulations, sell such Deposited Property at public or private sale, at such place or places and upon such terms as it may deem proper and may allocate the net proceeds of such sales (net of applicable (a) fees and charges of, and expenses incurred by, the Depositary and (b) taxes) for the account of the Holders otherwise entitled to such Deposited Property upon an averaged or other practicable basis without regard to any distinctions among such Holders and distribute the net proceeds so allocated to the extent practicable as in the case of a distribution received in cash pursuant to Section 4.1 of the Deposit Agreement. The Depositary shall not be responsible for (i) any failure to determine that it may be lawful or practicable to make such Deposited Property available to Holders in general or to any Holder in particular, (ii) any foreign exchange exposure or loss incurred in connection with such sale, or (iii) any liability to the purchaser of such Deposited Property.

(20) Exoneration. Nothwithstanding anything contained in the Deposit Agreement or any ADR, neither the Depositary nor the Company shall be obligated to do or perform any act which is inconsistent with the provisions of the Deposit Agreement or incur any liability (to the extent not limited by paragraph (25) hereof and Section 7.9 (b) of the Deposit Agreement) (i) if the Depositary, the Custodian, the Company or their respective agents shall be prevented or forbidden from, or delayed in, doing or performing any act or thing required or contemplated by the terms of the Deposit Agreement and this ADR, by reason of any provision of any present or future law or regulation of the United States, England and Wales or any other country, or of any other governmental authority or regulatory authority or stock exchange, or on account of potential criminal or civil penalties or restraint, or by reason of any provision, present or future, of the Articles of Association of the Company or any provision of or governing any Deposited Securities, or by reason of any act of God or war or other circumstances beyond its control (including, without limitation, nationalization, expropriation, currency restrictions, work stoppage, strikes, civil unrest, acts of terrorism, revolutions, rebellions, explosions and computer

failure), (ii) by reason of any exercise of, or failure to exercise, any discretion provided for in the Deposit Agreement or in the Articles of Association of the Company or provisions of or governing Deposited Securities, (iii) for any action or inaction in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Holder, any Beneficial Owner or authorized representative thereof, or any other person believed by it in good faith to be competent to give such advice or information, (iv) for the inability by a Holder or Beneficial Owner to benefit from any distribution, offering, right or other benefit which is made available to holders of Deposited Securities but is not, under the terms of the Deposit Agreement, made available to Holders of ADSs, (v) for any action or inaction of any clearing or settlement system (any participant thereof) for the Deposited Property or the ADSs, or (vi) for any consequential or punitive damages (including lost profits) for any breach of the terms of the Deposit Agreement. The Depositary, its controlling persons, its agents, any Custodian and the Company, its controlling persons and its agents may rely and shall be protected in acting upon any written notice, request or other document believed by it to be genuine and to have been signed or presented by the proper party or parties.

(21) **Standard of Care.** The Company and the Depositary assume no obligation and shall not be subject to any liability under the Deposit Agreement or this ADR to any Holder(s) or Beneficial Owner(s), except that the Company and the Depositary agree to perform their respective obligations specifically set forth in the Deposit Agreement or this ADR without negligence or bad faith. Without limitation of the foregoing, neither the Depositary, nor the Company, nor any of their respective controlling persons, or agents, shall be under any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Property or in respect of the ADSs, which in its opinion may involve it in expense or liability, unless indemnity satisfactory to it against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be required (and no Custodian shall be under any obligation whatsoever with respect to such proceedings, the responsibility of the Custodian being solely to the Depositary).

The Depositary and its agents shall not be liable for any failure to carry out any instructions to vote any of the Deposited Securities, or for the manner in which any vote is cast or the effect of any vote, provided that any such action or omission is in good faith and without negligence and in accordance with the terms of the Deposit Agreement. The Depositary shall not incur any liability for any failure to accurately determine that any distribution or action may be lawful or reasonably practicable, for the content of any information submitted to it by the Company for distribution to the Holders or for any inaccuracy of any translation thereof, for any investment risk associated with acquiring an interest in the Deposited Property, for the validity or worth of the Deposited Property, for any tax consequences that may result from the ownership of ADSs, Shares or other Deposited Property, for the credit-worthiness of any third party, for allowing any rights to lapse upon the terms of the Deposit Agreement, for the failure or timeliness of any notice from the Company, or for any action of or failure to act by, or any information provided or not provided by, DTC or any DTC Participant.

The Depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the Depositary or in connection with any matter arising wholly after the removal or resignation of the Depositary, provided that in connection with the issue out of which such potential liability arises the

Depositary performed its obligations without negligence or bad faith while it acted as Depositary.

(22) Resignation and Removal of the Depositary; Appointment of Successor Depositary. The Depositary may at any time resign as Depositary under the Deposit Agreement by written notice of resignation delivered to the Company, such resignation to be effective on the earlier of (i) the 90th day after delivery thereof to the Company (whereupon the Depositary shall be entitled to take the actions contemplated in Section 6.2 of the Deposit Agreement), or (ii) the appointment by the Company of a successor depositary and its acceptance of such appointment as provided in the Deposit Agreement. The Depositary may at any time be removed by the Company by written notice of such removal, which removal shall be effective on the later of (i) the 90th day after delivery thereof to the Depositary (whereupon the Depositary shall be entitled to take the actions contemplated in Section 6.2 of the Deposit Agreement), or (ii) upon the appointment by the Company of a successor depositary and its acceptance of such appointment as provided in the Deposit Agreement. In case at any time the Depositary acting hereunder shall resign or be removed, the Company shall use its best efforts to appoint a successor depositary, which shall be a bank or trust company having an office in the Borough of Manhattan, the City of New York. Every successor depositary shall be required by the Company to execute and deliver to its predecessor and to the Company an instrument in writing accepting its appointment hereunder, and thereupon such successor depositary, without any further act or deed (except as required by applicable law), shall become fully vested with all the rights, powers, duties and obligations of its predecessor (other than as contemplated in Sections 5.8 and 5.9 of the Deposit Agreement). The predecessor depositary, upon payment of all sums due it and on the written request of the Company shall (i) execute and deliver an instrument transferring to such successor all rights and powers of such predecessor hereunder (other than as contemplated in Sections 5.8 and 5.9 of the Deposit Agreement), (ii) duly assign, transfer and deliver all of the Depositary's right, title and interest to the Deposited Property to such successor, and (iii) deliver to such successor a list of the Holders of all outstanding ADSs and such other information relating to ADSs and Holders thereof as the successor may reasonably request. Any such successor depositary shall promptly provide notice of its appointment to such Holders. Any entity into or with which the Depositary may be merged or consolidated shall be the successor of the Depositary without the execution or filing of any document or any further act.

(23) Amendment/Supplement. Subject to the terms and conditions of this paragraph 23, and Section 6.1 of the Deposit Agreement and applicable law, this ADR and any provisions of the Deposit Agreement may at any time and from time to time be amended or supplemented by written agreement between the Company and the Depositary in any respect which they may deem necessary or desirable without the prior written consent of the Holders or Beneficial Owners. Any amendment or supplement which shall impose or increase any fees or charges (other than charges in connection with foreign exchange control regulations, and taxes and other governmental charges, delivery and other such expenses), or which shall otherwise materially prejudice any substantial existing right of Holders or Beneficial Owners, shall not, however, become effective as to outstanding ADSs until the expiration of thirty (30) days after notice of such amendment or supplement shall have been given to the Holders of outstanding ADSs. Notice of any amendment to the Deposit Agreement or any ADR shall not need to describe in detail the specific amendments effectuated thereby, and failure to describe the specific amendments in any such notice shall not render such notice invalid, provided, however, that, in

each such case, the notice given to the Holders identifies a means for Holders and Beneficial Owners to retrieve or receive the text of such amendment (*e.g.*, upon retrieval from the Commission's, the Depositary's or the Company's website or upon request from the Depositary). The parties hereto agree that any amendments or supplements which (i) are reasonably necessary (as agreed by the Company and the Depositary) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act or (b) the ADSs to be settled solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by Holders, shall be deemed not to materially prejudice any substantial existing rights of Holders or Beneficial Owners. Every Holder and Beneficial Owner at the time any amendment or supplement so becomes effective shall be deemed, by continuing to hold such ADSs, to consent and agree to such amendment or supplement and to be bound by the Deposit Agreement and this ADR, if applicable, as amended or supplemented thereby. In no event shall any amendment or supplement impair the right of the Holder to surrender such ADS and receive therefor the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law. Notwithstanding the foregoing, if any governmental body should adopt new laws, rules or regulations which would require an amendment of, or supplement to, the Deposit Agreement to ensure compliance therewith, the Company and the Depositary may amend or supplement the Deposit Agreement and this ADR at any time in accordance with such changed laws, rules or regulations. Such amendment or supplement to the Deposit Agreement and this ADR in such circumstances may become effective before a notice of such amendment or supplement is given to Holders or within any other period of time as required for compliance with such laws, rules or regulations.

(24) **Termination.** The Depositary shall, at any time at the written direction of the Company, terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. If ninety (90) days shall have expired after (i) the Depositary shall have delivered to the Company a written notice of its election to resign, or (ii) the Company shall have delivered to the Depositary a written notice of the removal of the Depositary, and, in either case, a successor depositary shall not have been appointed and accepted its appointment as provided in Section 5.4 of the Deposit Agreement, the Depositary may terminate the Deposit Agreement by distributing notice of such termination to the Holders of all ADSs then outstanding at least thirty (30) days prior to the date fixed in such notice for such termination. The date so fixed for termination of the Deposit Agreement in any termination notice so distributed by the Depositary to the Holders of ADSs is referred to as the "Termination Date". Until the Termination Date, the Depositary shall continue to perform all of its obligations under the Deposit Agreement, and the Holders and Beneficial Owners will be entitled to all of their rights under the Deposit Agreement. If any ADSs shall remain outstanding after the Termination Date, the Registrar and the Depositary shall not, after the Termination Date, have any obligation to perform any further acts under the Deposit Agreement, except that the Depositary shall, subject, in each case, to the terms and conditions of the Deposit Agreement, continue to (i) collect dividends and other distributions pertaining to Deposited Securities, (ii) sell Deposited Property received in respect of Deposited Securities, (iii) deliver Deposited Securities, together with any dividends or other distributions received with respect thereto and the net proceeds of the sale of any other Deposited Property, in exchange for ADSs surrendered to the Depositary (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the

account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (iv) take such actions as may be required under applicable law in connection with its role as Depositary under the Deposit Agreement. At any time after the Termination Date, the Depositary may sell the Deposited Property then held under the Deposit Agreement and shall after such sale hold un-invested the net proceeds of such sale, together with any other cash then held by it under the Deposit Agreement, in an un-segregated account and without liability for interest, for the pro rata benefit of the Holders whose ADSs have not theretofore been surrendered. After making such sale, the Depositary shall be discharged from all obligations under the Deposit Agreement except (i) to account for such net proceeds and other cash (after deducting, or charging, as the case may be, in each case, the fees and charges of, and expenses incurred by, the Depositary, and all applicable taxes or governmental charges for the account of the Holders and Beneficial Owners, in each case upon the terms set forth in Section 5.9 of the Deposit Agreement), and (ii) as may be required at law in connection with the termination of the Deposit Agreement. After the Termination Date, the Company shall be discharged from all obligations under the Deposit Agreement, except for its obligations to the Depositary under Sections 5.8, 5.9 and 7.6 of the Deposit Agreement. The obligations under the terms of the Deposit Agreement of Holders and Beneficial Owners of ADSs outstanding as of the Termination Date shall survive the Termination Date and shall be discharged only when the applicable ADSs are presented by their Holders to the Depositary for cancellation under the terms of the Deposit Agreement (except as specifically provided in the Deposit Agreement).

Notwithstanding anything contained in the Deposit Agreement or any ADR, in connection with the termination of the Deposit Agreement, the Depositary may, independently and without the need for any action by the Company, make available to Holders of ADSs a means to withdraw the Deposited Securities represented by their ADSs and to direct the deposit of such Deposited Securities into an unsponsored American depositary shares program established by the Depositary, upon such terms and conditions as the Depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored American depositary shares program under the Securities Act, and to receipt by the Depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the Depositary.

(25) Compliance with, and No Disclaimer under, U.S. Securities Laws. (a) Notwithstanding any provisions in this ADR or the Deposit Agreement to the contrary, the withdrawal or delivery of Deposited Securities will not be suspended by the Company or the Depositary except as would be permitted by Instruction I.A. (1) of the General Instructions to the Form F-6 Registration Statement, as amended from time to time, under the Securities Act.

(b) Each of the parties to the Deposit Agreement (including, without limitation, each Holder and Beneficial Owner) acknowledges and agrees that no provision of the Deposit Agreement or any ADR shall, or shall be deemed to, disclaim any liability under the Securities Act or the Exchange Act, in each case to the extent established under applicable U.S. laws.

(26) No Third Party Beneficiaries/Acknowledgements. The Deposit Agreement is for the exclusive benefit of the parties hereto (and their successors) and shall not be deemed to give any legal or equitable right, remedy or claim whatsoever to any other person, except to the extent specifically set forth in the Deposit Agreement. Nothing in the Deposit Agreement shall

be deemed to give rise to a partnership or joint venture among the parties nor establish a fiduciary or similar relationship among the parties. The parties hereto acknowledge and agree that (i) Citibank and its Affiliates may at any time have multiple banking relationships with the Company, the Holders, the Beneficial Owners, and their respective Affiliates, (ii) Citibank and its Affiliates may own and deal in any class of securities of the Company and its Affiliates and in ADSs, and may be engaged at any time in transactions in which parties adverse to the Company, the Holders, the Beneficial Owners or their respective Affiliates may have interests, (iii) the Depositary and its Affiliates may from time to time have in their possession non-public information about the Company, the Holders, the Beneficial Owners, and their respective Affiliates, (iv) nothing contained in the Deposit Agreement shall (a) preclude Citibank or any of its Affiliates from engaging in such transactions or establishing or maintaining such relationships, or (b) obligate Citibank or any of its Affiliates to disclose such information, transactions or relationships, or to account for any profit made or payment received in such transactions or relationships, (v) the Depositary shall not be deemed to have knowledge of any information any other division of Citibank or any of its Affiliates may have about the Company, the Holders, the Beneficial Owners, or any of their respective Affiliates, and (vi) the Company, the Depositary, the Custodian and their respective agents and controlling persons may be subject to the laws and regulations of jurisdictions other than the United States, England, and the authority of courts and regulatory authorities of such other jurisdictions, and, consequently, the requirements and the limitations of such other laws and regulations, and the decisions and orders of such other courts and regulatory authorities, may affect the rights and obligations of the parties to the Deposit Agreement.

(27) **Governing Law / Waiver of Jury Trial**. The Deposit Agreement, the ADRs and the ADSs shall be interpreted in accordance with, and all rights hereunder and thereunder and provisions hereof and thereof shall be governed by, the laws of the State of New York applicable to contracts made and to be wholly performed in that State. Notwithstanding anything contained in the Deposit Agreement to the contrary, any ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and the obligations and duties of the Company in respect of the holders of Shares and other Deposited Securities, as such, shall be governed by the laws of England and Wales (or, if applicable, such other laws as may govern the Deposited Securities).

EACH OF THE PARTIES TO THE DEPOSIT AGREEMENT (INCLUDING, WITHOUT LIMITATION, EACH HOLDER AND BENEFICIAL OWNER) IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING AGAINST THE COMPANY AND/OR THE DEPOSITARY ARISING OUT OF, OR RELATING TO, THE DEPOSIT AGREEMENT, ANY ADR AND ANY TRANSACTIONS CONTEMPLATED THEREIN (WHETHER BASED ON CONTRACT, TORT, COMMON LAW OR OTHERWISE).

(ASSIGNMENT AND TRANSFER SIGNATURE LINES)

FOR VALUE RECEIVED, the undersigned Holder hereby sell(s), assign(s) and transfer(s) unto whose taxpayer identification number is and whose address including postal zip code is , the within ADR and all rights thereunder, hereby irrevocably constituting and appointing attorney-in-fact to transfer said ADR on the books of the Depositary with full power of substitution in the premises.

Dated:

Name:

By:
Title:

NOTICE: The signature of the Holder to this assignment must correspond with the name as written upon the face of the within instrument in every particular, without alteration or enlargement or any change whatsoever.

If the endorsement be executed by an attorney, executor, administrator, trustee or guardian, the person executing the endorsement must give his/her full title in such capacity and proper evidence of authority to act in such capacity, if not on file with the Depositary, must be forwarded with this ADR.

SIGNATURE GUARANTEED

All endorsements or assignments of ADRs must be guaranteed by a member of a Medallion Signature Program approved by the Securities Transfer Association, Inc.

Legends

[The ADRs issued in respect of Partial Entitlement American Depositary Shares shall bear the following legend on the face of the ADR: "This ADR evidences ADSs representing 'partial entitlement' Shares of the Company and as such do not entitle the holders thereof to the same per-share entitlement as other Shares (which are 'full entitlement' Shares) issued and outstanding at such time. The ADSs represented by this ADR shall entitle holders to distributions and entitlements identical to other ADSs when the Shares represented by such ADSs become 'full entitlement' Shares."]

EXHIBIT B

FEE SCHEDULE

ADS FEES AND RELATED CHARGES

All capitalized terms used but not otherwise defined herein shall have the meaning given to such terms in the Deposit Agreement. Except as otherwise specified herein, any reference to ADSs herein includes Partial Entitlement ADSs, Full Entitlement ADSs, Certificated ADSs, Uncertificated ADSs, and Restricted ADSs.

I. ADS Fees

The following ADS fees are payable under the terms of the Deposit Agreement:

Service	Rate	By Whom Paid
(1) Issuance of ADSs (e.g., an issuance upon a deposit of Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason), excluding issuances as a result of distributions described in paragraph (4) below.	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) issued.	Person for whom ADSs are issued.
(2) Cancellation of ADSs (*e.g.*, a cancellation of ADSs for Delivery of deposited Shares, upon a change in the ADS(s)-to-Share(s) ratio, or for any other reason).	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) cancelled.	Person for whom ADSs are being cancelled.
(3) Distribution of cash dividends or other cash distributions (*e.g.*, upon a sale of rights and other entitlements).	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held.	Person to whom the distribution is made.
(4) Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) an exercise of rights to purchase additional ADSs.	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held.	Person to whom the distribution is made.
(5) Distribution of securities other than ADSs or rights to purchase additional ADSs (*e.g.*, spin-off shares).	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held.	Person to whom the distribution is made.

6) ADS Services.	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the Depositary.	Person holding ADSs on the applicable record date(s) established by the Depositary.
7) Registration of ADS Transfers (*e.g.*, upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and *vice versa*, or for any other reason).	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) transferred.	Person for whom or to whom ADSs are transferred.
8) Conversion of ADSs of one series for ADSs of another series (*e.g.*, upon conversion of Partial Entitlement ADSs for Full Entitlement ADSs, or upon conversion of Restricted ADSs into freely transferable ADSs, and *vice versa*).	Up to U.S. $5.00 per 100 ADSs (or fraction thereof) converted.	Person for whom ADSs are converted or to whom the converted ADSs are delivered.

II. Charges

The Company, Holders, Beneficial Owners, persons depositing Shares or withdrawing Deposited Securities in connection with ADS issuances and cancellations, and persons for whom ADSs are issued or cancelled shall be responsible for the following ADS charges under the terms of the Deposit Agreement:

(i) taxes (including applicable interest and penalties) and other governmental charges;

(ii) such registration fees as may from time to time be in effect for the registration of Shares or other Deposited Securities on the share register and applicable to transfers of Shares or other Deposited Securities to or from the name of the Custodian, the Depositary or any nominees upon the making of deposits and withdrawals, respectively;

(iii) such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the Deposit Agreement to be at the expense of the person depositing Shares or withdrawing Deposited Property or of the Holders and Beneficial Owners of ADSs;

(iv) in connection with the conversion of Foreign Currency, the fees, expenses, spreads, taxes and other charges of the Depositary and/or conversion service providers (which may be a division, branch or Affiliate of the Depositary). Such fees, expenses, spreads, taxes, and other charges shall be deducted from the Foreign Currency;

(v) any reasonable and customary out-of-pocket expenses incurred in such conversion and/or on behalf of the Holders and Beneficial Owners in complying with currency exchange control or other governmental requirements; and

(vi) the fees, charges, costs and expenses incurred by the Depositary, the Custodian, or any nominee in connection with the ADR program.

The above fees and charges may at any time and from time to time be changed by agreement between the Company and the Depositary.

Exhibit 5.1

Goodwin Procter (UK) LLP
100 Cheapside
London EC2V 6DY

goodwinlaw.com
+44 (0) 20 7447 4200

13 May 2019

Bicycle Therapeutics plc
Building 900
Babraham Research Campus
Babraham
Cambridgeshire
CB22 3AT

Ladies and Gentlemen:

Bicycle Therapeutics plc — Registration Statement on Form S-1 — Exhibit 5.1

We have acted as English legal advisers to Bicycle Therapeutics plc, a public limited company incorporated in England and Wales (the "**Company**") with company number 11036004 in connection with the proposed offering of American Depositary Shares (the "**ADSs**") representing ordinary shares of nominal value £0.01 each in the capital of the Company (the "**Ordinary Shares**") (the "**Offering**" and the Ordinary Shares allotted and issued in connection therewith to Citibank N.A. as the custodian and represented by ADSs, being the "**Shares**"). Each ADS represents one Ordinary Share of the Company.

1. INTRODUCTION

1.1 Purpose

In connection with the preparation and filing of a registration statement on Form S-1 (File No.333-231076) (such registration statement, as amended through the date hereof, the "**Registration Statement**"), to which this letter is attached as an exhibit, with the U.S. Securities and Exchange Commission (the "**SEC**") pursuant to the U.S. Securities Act of 1933, as amended (the "**Securities Act**"), we have been asked to provide opinions on certain matters, as set out below. We have taken instruction in this regard solely from the Company.

1.2 Defined terms and headings

In this letter:

(a) capitalised terms used without definition in this letter or the schedules hereto have the meanings assigned to them in the Registration Statement unless a contrary indication appears;

(b) headings are for ease of reference only and shall not affect interpretation; and

(c) the term "**Shares**" shall include any additional ADSs registered by the Company pursuant to Rule 462(b) under the Securities Act in connection with the Offering contemplated by the Registration Statement.

1.3 **Legal review**

For the purpose of issuing this letter, we have examined such questions of law as we have considered appropriate to give the opinions set forth in this letter. We have reviewed such documents and conducted such enquiries and searches as we have considered appropriate to give the opinions set forth in this letter, including the following documents and the following enquiries and searches:

(a) an online search at Companies House in respect of information available for inspection on the Company's file conducted on 13 May 2019 at 10.30 a.m. (London time);

(b) an enquiry of the Central Index of Winding Up Petitions, London on 13 May 2019 at 10.30 a.m. (London time) ((a) and (b) together, the "**Searches**");

(c) a PDF copy of the written resolutions passed by the shareholders of the Company in connection with the Offering (the "**Written Resolutions**");

(d) a PDF executed copy of the minutes of a meeting of the board of directors of Bicycle Therapeutics Limited (the "**Board Resolutions**") held on 25 April 2019 at which it was resolved, inter alia, to appoint a pricing committee of the board of directors of the Company (the "**Committee**");

(e) a PDF executed copy of the minutes of a meeting of the Committee at which it was resolved, inter alia, to allot the Shares (the "**Allotment Resolutions**" and together with the Board Resolutions and the Written Resolutions, the "**Corporate Approvals**");

(f) a PDF executed copy of a consent from certain shareholders in the Company comprising a "Preferred Majority" (as defined in the Company's articles of association in effect for the time being) dated 13 May 2019 approving, amongst other things, various matters relating to the Offering (the "**Investor Consent**");

(g) PDF executed copies of consents from the relevant class holders waiving any and all rights under the Current Articles (as defined below) and consenting to the conversion of the relevant classes of shares in the Company into a single class of ordinary shares (the "**Class Consents**");

(h) a PDF executed copy of a letter from the Investor Directors comprising an "**Investor Director Consent**" (each as defined in the Current Articles (as defined below)) consenting to certain matters relating to the Offering;

(i) a PDF copy of the current articles of association of the Company adopted on 21 December 2018 (the "**Current Articles**") and a certificate of incorporation of the Company dated 27 October 2017;

(j) a draft copy of the articles of association of the Company to be adopted conditional on the completion of the Offering pursuant to a special resolution passed as part of the Written Resolutions (the "**IPO Articles**"); and

(k) a copy of the Registration Statement, as amended.

1.4 **Applicable law**

This letter, the opinions given in it, and any non-contractual obligations arising out of or in connection with it and/or the opinions given in it, are governed by, and to be construed in accordance with, English law and relate only to English law as applied by the English courts, including the laws of the European Union to the extent having the force of law in England, as at today's date. In particular:

(a) we have not investigated the laws of any country other than England and we assume that no foreign law affects any of the opinions given below.;

(b) we do not undertake or accept any obligation to update this letter and/or the opinions given in it to reflect subsequent changes in English law or factual matters; and

(c) we express no opinion in this letter on the laws of any jurisdiction other than England. It is assumed that no foreign law which may apply to the matters contemplated by the Registration Statement, the Offering, the Company, any document or any other matter contemplated by any document would or might affect this letter and/or the opinions given in it.

1.5 **Assumptions and reservations**

The opinions given in this letter are given on the basis of each of the assumptions set out in paragraph 1.4, schedule 1 (*Assumptions*) and are subject to each of the reservations set out in schedule 2 (*Reservations*) to this letter. The opinions given in this letter are strictly limited to the matters stated in paragraph 2 (*Opinions*) below and do not extend, and should not be read as extending, by implication or otherwise, to any other matters.

2. OPINION

Subject to paragraph 1 (*Introduction*) and the other matters set out in this letter and its schedules, and subject further to the following:

(a) the Registration Statement becoming effective under the Securities Act;

(b) the number of Shares to be allotted and issued in connection with the Offering not being greater than 4,983,333 and such Shares being allotted and issued by 31 July 2019;

(c) that the Board Resolutions and the Allotment Resolutions were or will be (as appropriate) each passed at a meeting which was or will be duly convened and held in accordance with all applicable laws and regulations; that in particular, but without limitation, a duly qualified quorum of directors was or will be present in each case throughout the meeting and voted or will vote in favour of the resolutions; and that in relation to each meeting of the board of directors of the Company and of the Committee, each provision contained in the Companies Act 2006, as amended (the "**Act**") or the Current Articles relating to the declaration of the directors' interests or the power of the interested directors to vote and to count in the quorum was or will be duly observed;

(d) that the Written Resolutions were duly constituted and all constitutional, statutory and other formalities were duly observed, the requisite majority of shareholders, as applicable, voted in favour of approving the resolutions and the resolutions passed thereby were duly adopted, have not been revoked or varied and remain in full force and effect;

(e) the receipt in full of payment for the Shares in an amount of "cash consideration" (as defined in section 583(3) of the Act) of not less than the aggregate nominal value for such Shares; and

(f) valid entries having been made in relation to the allotment and issue of the Shares in the books and registers of the Company,

it is our opinion that, as at today's date, the Shares, if and when allotted and issued, registered in the name of the recipient in the register of members of the Company and delivered as described in the Registration Statement, will be duly and validly authorised and issued, fully paid or credited as fully paid (subject to the receipt of valid consideration by the Company for the issue thereof in connection with the Offering) and will not be subject to any call for payment of further capital.

3. EXTENT OF OPINIONS

We express no opinion as to any agreement, instrument or other document other than as specified in this letter or as to any liability to tax or duty which may arise or be suffered as a result of or in connection with the Offering or the transactions contemplated thereby.

This letter only applies to those facts and circumstances which exist as at today's date and we assume no obligation or responsibility to update or supplement this letter to reflect any facts or circumstances which may subsequently come to our attention, any changes in laws which may occur after today, or to inform the addressee of any change in circumstances happening after the date of this letter which would alter our opinion.

4. DISCLOSURE AND RELIANCE

This letter is addressed to you in connection with the Registration Statement. We consent to the filing of this letter as an exhibit to the Registration Statement. We further consent to the incorporation by reference of this letter and consent into any registration statement filed pursuant to Rule 462(b) under the Securities Act with respect to the Shares. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Other than for the purpose set out in the prior paragraph, this letter may not be relied upon, or assigned, for any purpose, without our prior written consent, which may be granted or withheld in our discretion.

Yours faithfully

/s/ Goodwin Procter (UK) LLP

Goodwin Procter (UK) LLP

SCHEDULE 1

ASSUMPTIONS

The opinions in this letter have been given on the basis of the following assumptions:

(a) the genuineness of all signatures, stamps and seals on all documents, the authenticity and completeness of all documents submitted to us as originals, and the conformity to original documents of all documents submitted to us as copies;

(b) that, where a document has been examined by us in draft or specimen form, it will be or has been duly executed in the form of that draft or specimen, and that each of the signed documents examined by us has been duly executed and, where applicable, delivered on behalf of the Company;

(c) that the articles of association of the Company referred to in paragraph 1.3(i) of this letter (the Current Articles) remain in full force and effect, and, save for the adoption of the IPO Articles upon the Offering, no alteration has been made or will be made to such articles of association, in each case prior to the date of allotment and issue of the Shares (the "Allotment Date");

(d) on the Allotment Date the Company will comply with all applicable laws to allot and issue the Shares and the Company will receive such amounts as are necessary to fully pay the nominal value of the Shares and any applicable share premium;

(e) that all documents, forms and notices which should have been delivered to the Registrar of Companies in respect of the Company have been so delivered, that information revealed by the Searches was complete and accurate in all respects and has not, since the time of the Searches, been altered and that the results of the Searches will remain complete and accurate as at the Allotment Date;

(f) that the Company has not taken any corporate or other action nor have any steps been taken or legal proceedings been started against the Company for the liquidation, winding up, dissolution, reorganisation or bankruptcy of, or for the appointment of a liquidator, receiver, trustee, administrator, administrative receiver or similar officer of, the Company or all or any of its assets (or any analogous proceedings in any jurisdiction) and the Company is not unable to pay its debts as they fall due within the meaning of section 123 of the Insolvency Act 1986, as amended, and will not become unable to pay its debts within the meaning of that section as a result of any of the transactions contemplated herein, is not insolvent and has not been dissolved or declared bankrupt;

(g) that the minutes of the meetings of the board of directors of the Company and the Committee provided to us in connection with the giving of the opinions in this letter reflect a true record of the proceedings described in them in duly convened, constituted and quorate meetings in which all constitutional, statutory and other formalities were duly observed, and the resolutions set out in the minutes were validly passed and have not been and will not be revoked or varied and remain in full force and effect and will remain so as at the Allotment Date;

(h) that the resolutions set out in the Written Resolutions and the Allotment Resolutions were validly passed and have not been and will not be revoked or varied and remain in full force and effect and will remain so as at the Allotment Date;

(i) that in relation to the allotment and issue of the Shares, the directors of the Company have acted and will act in the manner required by section 172 of the Act (Duty to promote the success of the Company), and there has not been and will not be any bad faith, breach of trust, fraud, coercion, duress or undue influence on the part of any of the directors of the Company;

(j) following the date of this letter and prior to the issue of the Ordinary Shares, the Company will validly enter into an underwriting agreement on substantially the terms and conditions described in Exhibit 1.1 of the Registration Statement;

(k) that no Shares or rights to subscribe for Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000, as amended ("FSMA") or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Shares in breach of section 21 of FSMA or any other United Kingdom laws or regulations relating to offers or invitations to subscribe for, or to acquire rights to subscribe for or otherwise acquire, shares or other securities; and

(l) the Company is not, nor will be, engaging in criminal, misleading, deceptive or unconscionable conduct or seeking to conduct any relevant transaction or any associated activity in a manner or for a purpose which might render any transaction contemplated under the Corporate Approvals or any associated activity illegal, void or voidable.

SCHEDULE 2

RESERVATIONS

The opinions in this letter are subject to the following reservations:

(a) the Searches are not capable of revealing conclusively whether or not a winding-up or administration petition or order has been presented or made, a receiver appointed, a company voluntary arrangement proposed or approved or any other insolvency proceeding commenced, and the available records may not be complete or up-to-date. In particular, the Central Registry of Winding-Up Petitions in England may not contain details of administration applications filed, or appointments recorded in or orders made by, district registries and county courts outside London. Searches at Companies House and at the Central Registry of Winding Up Petitions in England are not capable of revealing whether or not a winding up petition or a petition for the making of an administration order has been presented and, further, notice of a winding up order or resolution, notice of an administration order and notice of the appointment of a receiver may not be filed at Companies House immediately and there may be a delay in the relevant notice appearing on the file of the company concerned. Further, not all security interests are registrable, such security interests have not in fact been registered or such security interests have been created by an individual or an entity which is not registered in England. We have not made enquiries of any District Registry or County Court in England;

(b) the opinions set out in this letter are subject to: (i) any limitations arising from applicable laws relating to insolvency, bankruptcy, administration, reorganisation, liquidation, moratoria, schemes or analogous circumstances; and (ii) an English court exercising its discretion under section 426 of the Insolvency Act 1986 (*co-operation between courts exercising jurisdiction in relation to insolvency*) to assist the courts having the corresponding jurisdiction in any part of the United Kingdom or any relevant country or territory;

(c) we express no opinion as to matters of fact;

(d) we have only reviewed the documents listed in paragraph 2 (*Opinion*) above;

(e) we have made no enquiries of any individual connected with the Company;

(f) a certificate, documentation, notification, opinion or the like might be held by the English courts not to be conclusive if it can be shown to have an unreasonable or arbitrary basis or in the event of a manifest error; and

(g) it should be understood that we have not been responsible for investigating or verifying (i) the accuracy of the facts, including statements of foreign law, or the reasonableness of any statements of opinion, contained in the Registration Statement; or (ii) that no material facts have been omitted from it.

Exhibit 10.4

SENIOR EXECUTIVE CASH INCENTIVE BONUS PLAN

1. Purpose

This Senior Executive Cash Incentive Bonus Plan (the "Incentive Plan") is intended to provide an incentive for superior work and to motivate eligible executives of Bicycle Therapeutics Plc and its group companies (the "Company") and its subsidiaries toward even higher achievement and business results, to tie their goals and interests to those of the Company and its shareholders and to enable the Company to attract and retain highly qualified executives. The Incentive Plan is for the benefit of Covered Executives (as defined below).

2. Covered Executives

From time to time, the Compensation Committee of the Board of Directors of the Company (the "Compensation Committee") may select certain key executives (the "Covered Executives") to be eligible to receive bonuses hereunder. Participation in the Incentive Plan does not change the "at will" nature of a Covered Executive's employment with the Company.

3. Administration

The Compensation Committee shall have the sole discretion and authority to administer and interpret the Incentive Plan.

4. Bonus Determinations

(a) Corporate Performance Goals. A Covered Executive may receive a bonus payment under the Incentive Plan based upon the attainment of one or more performance objectives that are established by the Compensation Committee and relate to financial and operational metrics with respect to the Company or any of its subsidiaries (the "Corporate Performance Goals"), including the following: earnings before interest, taxes, depreciation and amortization; cash flow (including, but not limited to, operating cash flow and free cash flow); revenue; corporate revenue; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of the Company's ordinary shares; economic value-added; acquisitions or strategic transactions; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of the Company's ordinary shares; bookings, new bookings or renewals; sales or market shares; number of customers and / or collaboration partners / licensees of Company's products , number of new customers and / or collaboration partners / licensees of Company's products or customer references; operating income and/or net annual recurring revenue, any of which may be (A) measured in absolute terms or compared to any incremental increase, (B) measured in terms of growth, (C) compared to another company or companies or to results of a peer group, (D) measured against the market as a whole and/or as compared to applicable market indices and/or (E) measured on a pre-tax or post-tax basis (if applicable). Further, any Corporate Performance Goals may be used to measure the performance of the Company as a whole or a business unit or other segment of the Company, or one or more product

lines or specific markets. The Corporate Performance Goals may differ from Covered Executive to Covered Executive.

(b) Calculation of Corporate Performance Goals. At the beginning of each applicable performance period, the Compensation Committee will determine whether any significant element(s) will be included in or excluded from the calculation of any Corporate Performance Goal with respect to any Covered Executive. In all other respects, Corporate Performance Goals will be calculated in accordance with the Company's financial statements, generally accepted accounting principles, or under a methodology established by the Compensation Committee at the beginning of the performance period and which is consistently applied with respect to a Corporate Performance Goal in the relevant performance period.

(c) Target; Minimum; Maximum. Each Corporate Performance Goal shall have a "target" (i.e., 100 percent attainment of the Corporate Performance Goal) and may also have a "minimum" hurdle and/or a "maximum" amount.

(d) Bonus Requirements; Individual Goals. Except as otherwise set forth in this Section 4(d): (i) any bonuses paid to Covered Executives under the Incentive Plan shall be based upon objectively determinable bonus formulas that tie such bonuses to one or more performance targets relating to the Corporate Performance Goals, (ii) bonus formulas for Covered Executives shall be adopted in each performance period by the Compensation Committee and communicated to each Covered Executive at the beginning of each performance period and (iii) no bonuses shall be paid to Covered Executives unless and until the Compensation Committee makes a determination with respect to the attainment of the performance targets relating to the Corporate Performance Goals. Notwithstanding the foregoing, the Compensation Committee may adjust bonuses payable under the Incentive Plan based on achievement of one or more individual performance objectives or pay bonuses (including, without limitation, discretionary bonuses) to Covered Executives under the Incentive Plan based on individual performance goals and/or upon such other terms and conditions as the Compensation Committee may in its discretion determine.

(e) Individual Target Bonuses. The Compensation Committee shall establish a target bonus opportunity for each Covered Executive for each performance period. For each Covered Executive, the Compensation Committee shall have the authority to apportion the target award so that a portion of the target award shall be tied to attainment of Corporate Performance Goals and a portion of the target award shall be tied to attainment of individual performance objectives.

(f) Employment Requirement. Subject to any additional terms contained in a written agreement between the Covered Executive and the Company, the payment of a bonus to a Covered Executive with respect to a performance period shall be conditioned upon the Covered Executive's employment by the Company on the bonus payment date. If a Covered Executive was not employed for an entire performance period, the Compensation Committee may pro rate the bonus based on the number of days employed during such period.

5. Timing of Payment

(a) With respect to Corporate Performance Goals established and measured on a basis more frequently than annually (e.g., quarterly or semi-annually), the Corporate Performance

Goals will be measured at the end of each performance period after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for such period are met, payments will be made as soon as practicable following the end of such period, but not later 74 days after the end of the fiscal year in which such performance period ends.

(b) With respect to Corporate Performance Goals established and measured on an annual or multi-year basis, Corporate Performance Goals will be measured as of the end of each such performance period (e.g., the end of each fiscal year) after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for any such period are met, bonus payments will be made as soon as practicable, but not later than 74 days after the end of the relevant fiscal year.

(c) For the avoidance of doubt, bonuses earned at any time in a fiscal year must be paid no later than 74 days after the last day of such fiscal year.

6. Amendment and Termination

The Company reserves the right to amend or terminate the Incentive Plan at any time in its sole discretion.

Exhibit 10.5

BICYCLE THERAPEUTICS PLC

2019 EMPLOYEE SHARE PURCHASE PLAN

The purpose of the Bicycle Therapeutics plc 2019 Employee Share Purchase Plan (the "**Plan**") is to provide eligible employees of Bicycle Therapeutics plc (the "**Company**") and each Designated Subsidiary (as defined in Section 11) with opportunities to purchase Shares. 215,000 Shares in the aggregate have been approved and reserved for this purpose, plus on January 1, 2020 and each January 1 thereafter through January 1, 2029, the number of Shares reserved and available for issuance under the Plan shall be cumulatively increased by the lower of: (i) 430,000 Ordinary Shares; (ii) one percent (1%) of the number of Shares issued and outstanding on the immediately preceding December 31; or (iii) such lesser number of Shares as determined by the Compensation Committee The Plan is intended to constitute an "employee stock purchase plan" within the meaning of Section 423(b) of the U.S. Internal Revenue Code of 1986, as amended (the "**U.S. Code**"), and shall be interpreted in accordance with that intent.

1. Administration. The Plan will be administered by the Compensation Committee as appointed by the Company's Board of Directors (the "**Board**") from time to time. The Compensation Committee has authority at any time to: (i) adopt, alter and repeal such rules, guidelines and practices for the administration of the Plan and for its own acts and proceedings as it shall deem advisable; (ii) interpret the terms and provisions of the Plan; (iii) make all determinations it deems advisable for the administration of the Plan; (iv) decide all disputes arising in connection with the Plan; and (v) otherwise supervise the administration of the Plan. All interpretations and decisions of the Compensation Committee shall be binding on all persons, including the Company and the Participants. No member of the Board or individual exercising administrative authority with respect to the Plan shall be liable for any action or determination made in good faith with respect to the Plan or any option granted hereunder.

2. Offerings. The Company will make one or more offerings to eligible employees to purchase Shares under the Plan ("**Offerings**") provided that no Offering may be made at any time if it would be unlawful, or in breach of any regulation or guidance with which the Company complies including the rules of any investment exchange on which the Company's shares are listed or traded. The Compensation Committee shall determine when the initial Offering begins and ends (the "**Initial Offering**"). Thereafter, unless otherwise determined by the Compensation Committee, an Offering will begin on the first business day occurring on or after each June 1 and December 1 and will end on the last business day occurring on or before the following November 30 and May 31, respectively. The Compensation Committee may, in its discretion, designate a different period for any Offering, provided that no Offering shall exceed 27 months in duration or overlap any other Offering.

3. Eligibility. All individuals classified as employees on the payroll records of the Company and each Designated Subsidiary are eligible to participate in any one or more of the Offerings under the Plan, provided that as of the first day of the applicable Offering (the "**Offering Date**") they are customarily employed by the Company or a Designated Subsidiary for more than 20 hours a week and have completed at least three months of employment. Notwithstanding any other provision herein, individuals who are not contemporaneously classified as employees of the Company or a Designated Subsidiary for purposes of the Company's or applicable Designated Subsidiary's payroll system are not considered to be eligible employees of the Company or any Designated Subsidiary and shall not be eligible to participate in the Plan. In the event any such individuals are reclassified as employees of the Company or a Designated Subsidiary for any purpose, including, without limitation, common law or statutory employees, by any action of any third party, including, without limitation, any

government agency, or as a result of any private lawsuit, action or administrative proceeding, such individuals shall, notwithstanding such reclassification, remain ineligible for participation. Notwithstanding the foregoing, the exclusive means for individuals who are not contemporaneously classified as employees of the Company or a Designated Subsidiary on the Company's or Designated Subsidiary's payroll system to become eligible to participate in this Plan is through an amendment to this Plan, duly executed by the Company, which specifically renders such individuals eligible to participate herein.

4. Participation.

(a) Participants on Effective Date. Each eligible employee as of the Registration Date shall be deemed to be a Participant at such time. If an eligible employee is deemed to be a Participant pursuant to this Section 4(a), such individual shall be deemed not to have authorized payroll deductions and shall not purchase any Shares hereunder unless he or she thereafter authorizes payroll deductions by submitting an enrolment form (in the manner described in Section 4(c)) within 60 days of the commencement of the Initial Offering. If such a Participant does not authorize payroll deductions by submitting an enrolment form within 60 days of the commencement of the Initial Offering, that Participant will be deemed to have withdrawn from the Plan.

(b) An eligible employee who is not a Participant in any prior Offering may participate in a subsequent Offering by submitting an enrolment form to his or her appropriate payroll location at least 15 business days before the Offering Date (or by such other deadline as shall be established by the Compensation Committee for the Offering).

(c) Enrolment. The enrolment form will (a) state a whole percentage or the amount to be deducted from an eligible employee's Compensation (as defined in Section 11) per pay period, (b) authorize the purchase of Shares in each Offering in accordance with the terms of the Plan and (c) specify the exact name or names in which Shares purchased for such individual are to be issued pursuant to Section 10. An employee who does not enrol in accordance with these procedures will be deemed to have waived the right to participate. Unless a Participant files a new enrolment form or withdraws from the Plan, such Participant's deductions and purchases will continue at the same percentage or amount of Compensation for future Offerings, provided he or she remains eligible.

(d) Notwithstanding the foregoing, participation in the Plan will neither be permitted nor be denied contrary to the requirements of the U.S. Code.

5. Employee Contributions. Each eligible employee may authorize payroll deductions at a minimum of 1 percent up to a maximum of 15 percent of such employee's Compensation for each pay period. The Company will maintain book accounts showing the amount of payroll deductions made by each Participant for each Offering. No interest will accrue or be paid on payroll deductions.

6. Deduction Changes. Except in the event of a Participant increasing his or her payroll deduction from 0 percent during the first Offering as specified in Section 4(a) as may be determined by the Compensation Committee in advance of an Offering, a Participant may not increase or decrease his or her payroll deduction during any Offering, but may increase or decrease his or her payroll deduction with respect to the next Offering (subject to the limitations of Section 5) by filing a new enrolment form at least 15 business days before the next Offering Date (or by such other deadline as shall be established by the Compensation Committee for the Offering). The Compensation Committee may, in advance of any Offering, establish rules permitting a Participant to increase, decrease or terminate his or her payroll deduction during an Offering.

7. Withdrawal. A Participant may withdraw from participation in the Plan by delivering a written notice of withdrawal to his or her appropriate payroll location. The Participant's withdrawal will be effective as of the next business day. Following a Participant's withdrawal, the Company will promptly refund such individual's entire account balance under the Plan to him or her (after payment for any Shares purchased before the effective date of withdrawal). Partial withdrawals are not permitted. Such an employee may not begin participation again during the remainder of the Offering, but may enrol in a subsequent Offering in accordance with Section 4.

8. Grant of Options. On each Offering Date, the Company will grant to each eligible employee who is then a Participant in the Plan an option ("**Option**") to purchase on the last day of such Offering (the "**Exercise Date**"), at the Option Price hereinafter provided for, the lowest of: (a) a number of Shares determined by dividing such Participant's accumulated payroll deductions on such Exercise Date by the lower of: (i) 85 percent of the Fair Market Value of the Shares on the Offering Date; or (ii) 85 percent of the Fair Market Value of the Shares on the Exercise Date; (b) a number of Shares determined dividing $25,000 by the Fair Market Value of the Shares on the Offering Date; or (c) such other lesser maximum number of Shares as shall have been established by the Compensation Committee in advance of the Offering; provided, however, that such Option shall be subject to the limitations set forth below. Each Participant's Option shall be exercisable only to the extent of such Participant's accumulated payroll deductions on the Exercise Date.

The purchase price for each share purchased under each Option (the "**Option Price**") will be 85 percent of the Fair Market Value of the Shares on the Offering Date or the Exercise Date, whichever is less.

Notwithstanding the foregoing, no Participant may be granted an option hereunder if such Participant, immediately after the option was granted, would be treated as owning shares possessing 5 percent or more of the total combined voting power or value of all classes of shares of the Company or any Parent or Subsidiary (as defined in Section 11). For purposes of the preceding sentence, the attribution rules of Section 424(d) of the U.S. Code shall apply in determining the share ownership of a Participant, and all shares which the Participant has a contractual right to purchase shall be treated as shares owned by the Participant. In addition, no Participant may be granted an Option which permits his or her rights to purchase Shares under the Plan, and any other employee share purchase plan of the Company and its Parents and Subsidiaries, to accrue at a rate which exceeds $25,000 of the fair market value of such Shares (determined on the option grant date or dates) for each calendar year in which the Option is outstanding at any time. The purpose of the limitation in the preceding sentence is to comply with Section 423(b)(8) of the U.S. Code and shall be applied taking Options into account in the order in which they were granted.

9. Exercise of Option and Purchase of Shares. Provided it would not then be in breach of the any applicable restriction, each employee who continues to be a Participant in the Plan on the Exercise Date shall be deemed to have exercised his or her Option on such date and shall acquire from the Company such number of whole Shares reserved for the purpose of the Plan as his or her accumulated payroll deductions on such date will purchase at the Option Price, subject to any other limitations contained in the Plan. Any amount remaining in a Participant's account at the end of an Offering solely by reason of the inability to purchase a fractional share will be carried forward to the next Offering; any other balance remaining in a Participant's account at the end of an Offering will be refunded to the Participant promptly.

10. Issuance of Certificates. Certificates representing Shares purchased under the Plan may be issued only in the name of the employee, in the name of the employee and

another person of legal age as joint tenants with rights of survivorship, or in the name of a broker authorized by the employee to be his, her or their, nominee for such purpose.

11. Definitions.

The term "**ADSs**" means American Depositary Shares, representing Ordinary Shares on deposit with a U.S. banking institution selected by the Company.

The term "**Compensation**" means the amount of base pay, prior to salary reduction pursuant to Sections 125, 132(f) or 401(k) of the U.S. Code, but excluding overtime, commissions, incentive or bonus awards, allowances and reimbursements for expenses such as relocation allowances or travel expenses, income or gains on the exercise of Company share options, and similar items.

The term "**Designated Subsidiary**" means any present or future Subsidiary (as defined below) that has been designated by the Board to participate in the Plan. The Board may so designate any Subsidiary, or revoke any such designation, at any time and from time to time, either before or after the Plan is approved by the shareholders. The current list of Designated Subsidiaries is attached hereto as Appendix A.

The term "**Fair Market Value of the Shares**" on any given date means the fair market value of the Shares determined in good faith by the Compensation Committee; provided, however, that if the ADSs are admitted to quotation on the National Association of Securities Dealers Automated Quotation System ("**NASDAQ**"), NASDAQ Global Market or another national securities exchange, the determination shall be made by reference to the closing price on such date. If there is no closing price for such date, the determination shall be made by reference to the last date preceding such date for which there is a closing price. Notwithstanding the foregoing, if the date for which the Fair Market Value of the Shares is determined is the Registration Date, the Fair Market Value of the Shares shall be determined based upon the "Price to the Public" (or equivalent) set forth on the cover page for the final prospectus relating to the Company's initial public offering.

The term "**Parent**" means a "parent corporation" with respect to the Company, as defined in Section 424(e) of the U.S. Code.

The term "**Ordinary Shares**" mean ordinary shares in the Company, with a nominal value of £0.01 per share.

The term "**Participant**" means an individual who is eligible as determined in Section 3 and who has complied with the provisions of Section 4.

The term "**Registration Date**" means the date upon which the registration statement on Form S-1 that is filed by the Company with respect to its initial public offering is declared effective by the Securities and Exchange Commission

The term "**Share**" means an Ordinary Share and/or the number of ADSs equal to an Ordinary Share, as the context may require

The term "**Subsidiary**" means a "subsidiary corporation" with respect to the Company, as defined in Section 424(f) of the U.S. Code.

12. Rights on Termination of Employment. If a Participant's employment terminates for any reason before the Exercise Date for any Offering, no payroll deduction will be taken from any pay due and owing to the Participant and the balance in the Participant's account will be paid to such Participant or, in the case of such Participant's death, to his or her

designated beneficiary as if such Participant had withdrawn from the Plan under Section 7. In the case of Participants who are employed in the UK, the termination date of their employment will be the date they give, or are given, notice of termination of their employment unless the Compensation Committee decides that it shall be a later date before the statutory or contractual expiry date of their notice period. An employee will be deemed to have terminated employment, for this purpose, if the corporation that employs him or her, having been a Designated Subsidiary, ceases to be a Subsidiary, or if the employee is transferred to any corporation other than the Company or a Designated Subsidiary. An employee will not be deemed to have terminated employment for this purpose, if the employee is on an approved leave of absence for military service or sickness or for any other purpose approved by the Company, if the employee's right to reemployment is guaranteed either by a statute or by contract or under the policy pursuant to which the leave of absence was granted or if the Compensation Committee otherwise provides in writing.

If a Participant ceases to be employed by the Company or any Subsidiary for any reason whatsoever (including as a result of being wrongfully or unfairly dismissed) they shall not be entitled, and by participating in this Plan they shall be deemed to have waived any possible entitlement, to any sum or benefit accrued or in prospect as a result of that participation and no such loss or curtailment shall form part of any claim for damages for breach of the Participant's contract of employment or compensation for dismissal or any other claim whatsoever.

13. Special Rules. Notwithstanding anything herein to the contrary, the Compensation Committee may adopt special rules applicable to the employees of a particular Designated Subsidiary, whenever the Compensation Committee determines that such rules are necessary or appropriate for the implementation of the Plan in a jurisdiction where such Designated Subsidiary has employees; provided that such rules are consistent with the requirements of Section 423(b) of the U.S. Code. Any special rules established pursuant to this Section 13 shall, to the extent possible, result in the employees subject to such rules having substantially the same rights as other Participants in the Plan.

14. Optionees Not Shareholders. Neither the granting of an Option to a Participant nor the deductions from his or her pay shall constitute such Participant a holder of the Shares covered by an Option under the Plan until such Shares have been purchased by and issued to him or her.

15. Rights Not Transferable. Rights under the Plan are not transferable by a Participant other than by will or the laws of descent and distribution, and are exercisable during the Participant's lifetime only by the Participant.

16. Application of Funds. All funds received or held by the Company under the Plan may be combined with other corporate funds and may be used for any corporate purpose.

17. Adjustment in Case of Changes Affecting Shares. In the event of a subdivision of outstanding Shares, the payment of a dividend in Shares or any other change affecting the Shares, the number of Shares approved for the Plan and the share limitation set forth in Section 8 shall be equitably or proportionately adjusted to give proper effect to such event.

18. Amendment of the Plan. The Board may at any time and from time to time amend the Plan in any respect, except that without the approval within 12 months of such Board action by the shareholders, no amendment shall be made increasing the number of Shares approved for the Plan or making any other change that would require shareholder approval in order for the Plan, as amended, to qualify as an "employee stock purchase plan" under Section 423(b) of the U.S. Code.

19. Insufficient Shares. If the total number of Shares that would otherwise be purchased on any Exercise Date plus the number of Shares purchased under previous Offerings under the Plan exceeds the maximum number of Shares issuable under the Plan, the Shares then available shall be apportioned among Participants in proportion to the amount of payroll deductions accumulated on behalf of each Participant that would otherwise be used to purchase Shares on such Exercise Date.

20. Termination of the Plan. The Plan may be terminated at any time by the Board. Upon termination of the Plan, all amounts in the accounts of Participants shall be promptly refunded. The Plan shall automatically terminate on the ten year anniversary of the Registration Date.

21. Governmental Regulations. The Company's obligation to sell and deliver Shares under the Plan is subject to obtaining all governmental approvals required in connection with the authorization, issuance, or sale of such Shares.

22. Governing Law. This Plan and all Options and actions taken thereunder shall be governed by, and construed in accordance with, the law of England and Wales, applied without regard to conflict of law principles.

23. Issuance of Shares. Shares may be issued upon exercise of an Option from authorized but unissued Shares, from Shares held in the treasury of the Company, or from any other proper source.

24. Tax Withholding. Participation in the Plan is subject to any minimum required tax withholding on income of the Participant in connection with the Plan. Each Participant agrees, by entering the Plan, that the Company and its Subsidiaries shall have the right to deduct any such taxes from any payment of any kind otherwise due to the Participant, including Shares issuable under the Plan. For this purposes "tax" shall mean Federal, state and local taxes and social security taxes in the US, and their equivalent in any other jurisdiction, for which a Participant is liable by reason of the acquisition, holding or disposal of Shares under the Plan or the receipt of any other benefit in connection with it and which the Company or any Subsidiary is liable to account for on the Participant's behalf.

25. Notification Upon Sale of Shares. Each Participant agrees, by entering the Plan, to give the Company prompt notice of any disposition of Shares purchased under the Plan where such disposition occurs within two years after the date of grant of the Option pursuant to which such Shares were purchased or within one year after the date such Shares were purchased.

26. Effective Date and Approval of Shareholders. The Plan shall take effect upon the date immediately preceding the Registration Date following shareholder approval in accordance with applicable law.

APPENDIX A

Designated Subsidiaries

BicycleRD Limited
BicycleTx Limited
Bicycle Therapeutics, Inc.

Exhibit 10.6

BICYCLE THERAPEUTICS PLC

RULES OF
THE BICYCLE THERAPEUTICS SHARE OPTION PLAN

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London EC4A 1BL
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CONTENTS

RULES OF THE BICYCLE THERAPEUTICS SHARE OPTION PLAN

1 DEFINITIONS AND INTERPRETATION

Definitions

1.1 The following definitions shall apply for the purposes of this Plan:

"Cessation Date"

in relation to an Optionholder who is an Employee means the date notice of termination of his employment is given by or to him unless the Compensation Committee in their absolute discretion determines a later date, not being later than the statutory or contractual expiry date of the applicable notice period;

"Change of Control"

as defined in Rule 10.1;

"Code"

the U.S. Internal Revenue Code of 1986, as amended, and any successor Code, and related rules, regulations and interpretations;

"Company"

Bicycle Therapeutics Plc registered in England with number 11036004;

"Compensation Committee"

the committee of the board of the Company constituted for the purpose of, amongst other matters, discharging the board of the Company's responsibility relating to compensation of the Company's directors and executives, save that in the event such committee has not been constituted, the board of the Company;

"Consultant"

an individual who provides consultancy services to a Group Company (which, for the avoidance of doubt, shall include any person who is: (a) directly engaged by a Group Company; and (b) employed by a third party to work in the provision of services to a Group Company on behalf of such third party who is engaged by a Group Company to provide such services);

"Control"

the meaning in section 995 of the Income Tax Act 2007;

"Corporate Event"

an event within Rule 10;

"Date of Grant"

the date on which an Option is granted under this Plan;

"Eligible Person"

an Employee or Consultant;

"Employee"

an Eligible Person who is or was a director, secretary or employee of a Group Company;

"Employer Company"

in the case of an Optionholder who is an Employee, the Optionholder's employer or former employer as applicable;

“Exercise Price”

the price determined in accordance with Rule 2.4 at which each Share subject to an Option may be acquired on the exercise of that Option:

“Financial Year”

the accounting reference period (as defined by the Companies Act 2006) of the Company;

“Fully Diluted Share Capital”

at the relevant time, the aggregate of: (a) the number of Shares in issue; and (b) the number of additional Shares which would be issued assuming the allotment and issue of the number of Shares in the Option Pool (whether or not on their terms the securities are actually convertible into Ordinary Shares at such time) only to the extent that such Shares are not already included in part (a) of this definition;

“Good Leaver”

ceasing to be an Employee or Consultant for one of the reasons in Rule 6.3;

“Group”

the Company, any company which is the Company’s subsidiary, its holding company or a subsidiary of its holding company (as “**subsidiary**” and “**holding company**” are defined in section 1159 of the UK Companies Act 2006) and “**Group Company**” shall be construed accordingly;

“HMRC”

Her Majesty’s Revenue & Customs;

“Incentive Stock Option”

any Option designated and qualified as an “incentive stock option” as defined in Section 422 of the Code;

“Market Value”

the market value of the shares subject to an Option determined in accordance with the applicable provisions of Part VIII of the Taxation of Chargeable Gains Act 1992; provided, however, that the Market Value for an Option granted to a U.S. Eligible Person shall be the closing market price on the Nasdaq Global Market (or such other market on which the Company’s Shares are then principally listed) of one Share on the effective date of grant, or if no closing price is reported for such date, the closing price on the next immediately following date for which a closing price is reported;

“Non-Qualified Stock Option”

any Option that is not an Incentive Stock Option;

“Normal Vesting Date”

the date specified in Rule 6.1 on which an Option may normally first be exercised;

“Option”

a right to acquire Shares granted under the Plan;

“Option Certificate”

a certificate setting out the terms of an Option issued in accordance with Rule 2.4;

"Option Pool"

the pool of Shares: (a) over which options have or may be granted to Eligible Persons under this Plan or any other plan; and (b) allotted and issued to Eligible Persons under any other arrangement;

"Optionholder"

an Eligible Employee who has been granted an Option under this Plan (including his personal representatives or beneficiaries in the event of his death):

"Performance Condition"

any objective condition(s) imposed in accordance with Rule 4.1 or any amended condition(s) substituted in accordance with Rule 4.2.

"Plan"

the Bicycle Therapeutics Share Option Plan constituted and governed by these Rules as amended from time to time;

"Scheme of Arrangement"

as defined in Rule 10.2;

"Shares"

ordinary shares in the Company;

"Ten Percent Owner"

an employee that resides in the US who owns or is deemed to own (by reason of the attribution rules of Section 424(d) of the Code) more than 10 percent of the combined voting power of all classes of shares of the Company or any parent or subsidiary corporation;

"U.S."

United States of America; and

"Vest"

subject to Rule 6.4 (*lapse of options*), the extent to which an Option becomes capable of exercise on the first to occur of:

(a) the Normal Vesting Date;

(b) the date of the Optionholder's death or the Cessation date of his employment within, or provision of consultancy services to, the Group as a Good Leaver; and

(c) a Corporate Event,

and "**Vested**" and "**Unvested**" shall be construed accordingly.

Interpretation

1.2 Headings are for reference purposes only and shall not affect the construction of these Rules.

1.3 References to any statutory provision are to that provision as amended, previously enacted, re-enacted or consolidated.

1.4 Where the context permits words in the singular shall include the plural and the masculine shall include the feminine and vice versa.

2 GRANT OF OPTIONS

Type of option

2.1 The Company may grant Options to any Eligible Employee it chooses provided that Incentive Stock Options may be granted only to Employees of the Company or any subsidiary that is a "subsidiary corporation" within the meaning of Section 424(f) of the Code. To the extent that any Option does not qualify as an Incentive Stock Option, it shall be deemed a Non-Qualified Stock Option.

When options may normally be granted

2.2 The Company may grant Options to any Eligible Employee it chooses:

(a) during the period of 42 days after the date the Plan is adopted by the Company; and

(b) at any other time the Compensation Committee decides that exceptional circumstances have arisen which justify the grant of Options.

When options may be granted

2.3 Options may be granted to any Eligible Person the Company chooses:

(a) at any time when that grant would not be prohibited by, or in breach of:

(i) any law;

(ii) any other regulation with the force of law; or

(iii) the rules of any investment exchange on which Shares are listed or traded, or any other non-statutory rule that binds the Company or with which the Compensation Committee has resolved to comply; and

(b) before the tenth anniversary of the Adoption Date.

Exercise price

2.4 Subject to Rule 12 (*variation of share capital*), the Exercise Price per Share may not be less than the higher of:

(a) if Shares are to be newly issued to satisfy the exercise of Options, the nominal value of a Share; and

(b) the Market Value of a Share on the Date of Grant.

In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the option price of such Incentive Stock Option shall be not less than 110 percent of the Market Value on the grant date.

Option certificates

2.5 An Option shall be granted by the Company executing an Option Certificate as a deed in a form approved by the Compensation Committee. Each Option Certificate shall state:

(a) the Date of Grant of the Option;

(b) the number and class of the Shares subject to the Option;

(c) the Exercise Price;

(d) the Normal Vesting Date;

(e) any applicable Performance Conditions imposed in accordance with Rule 4.1;

(f) the date when the Option will lapse (being not be later than the tenth anniversary of the Date of Grant);

(g) the date on which the Option was granted; and

(h) if the Compensation Committee so determines, such obligations on the part of the Optionholder as shall be deemed necessary to comply with any tax or securities laws

or other regulatory issues in any jurisdiction which may apply to the Company, any other Group Company, the Optionholder or any other person.

2.6 The Option Certificate is subject to the terms and conditions of this Plan.

3 NON-TRANSFERABILITY

Other than where Options are transferred or assigned to an Optionholder's personal representatives or beneficiary in the event of the Optionholder's death or pursuant to a domestic relations order, Options may not be transferred, assigned, pledged or charged and any purported transfer, assignment, pledge or charge shall cause the Option to lapse immediately. Each Option Certificate shall carry a statement to this effect.

4 PERFORMANCE CONDITIONS

Imposition of performance conditions

4.1 The exercise of an Option may be conditional upon the satisfaction of one or more objective Performance Condition(s) imposed by the Compensation Committee at the Date of Grant and specified in the Option Certificate.

Variation and waiver of performance conditions

4.2 If, after the Compensation Committee has determined any objective Performance Condition(s) to be satisfied pursuant to this Rule, events occur which cause the Compensation Committee to consider that any of the existing Condition(s) has become unfair or impractical, they may in their absolute discretion amend, relax or waive such Condition.

Notification to Optionholders

4.3 The Compensation Committee shall notify all relevant Optionholders in writing of any amendment, relaxation or waiver of existing targets or conditions made pursuant to Rule 4.2.

5 PLAN LIMITS

5.1 The number of Shares in the Option Pool at the Adoption Date shall be 10% of the Fully Diluted Share Capital, subject to adjustment per Section 12.

5.2 Thereafter, on the first day of each new Financial Year following the Adoption Date , until such time as the Compensation Committee otherwise determines, the number of Shares in the Option Pool shall be cumulatively increased by 4% of the number of Shares outstanding as of the day prior to the first day of the applicable new Financial Year (or such lesser amount as determined by the Board) (the "**Annual Increase**").

Inclusion of treasury shares

5.3 For the purposes of this Rule, any Shares which are treasury shares within sections 724 - 732 of the Companies Act 2006 shall be treated as though they were unissued Shares.

Exclusion of certain Shares

5.4 For the purposes of this Rule any Shares which are not treasury shares within Rule 5.2 and:

(a) which are already in issue when any option or other right is granted over them; or

(b) which were comprised in any option or other right to the extent that it has lapsed or been surrendered,

shall be disregarded.

ISO Limitation

5.5 Subject to such overall limitations set forth above, no more than 2,470,583 Shares may be issued in the form of Incentive Stock Options, increased on the first day of each new Financial Year following the Adoption Date, by the lesser of 430,000 Shares or the Annual Increase.

5.6 Annual Limit on Incentive Stock Options. To the extent required for "incentive stock option" treatment under Section 422 of the Code, the aggregate Market Value (determined as of the time of grant) of the shares with respect to which Incentive Stock Options granted under this Plan and any other plan of the Company or its parent and subsidiary corporations become exercisable for the first time by an Optionholder during any calendar year shall not exceed U.S. $100,000. To the extent that any Option exceeds this limit, it shall constitute a Non-Qualified Stock Option.

6 VESTING, EXERCISE AND LAPSE OF OPTIONS

Vesting of options

6.1 Save as provided in Rules 6.2 (*death of the Optionholder*), 6.3 (*cessation of employment or consultancy as a good leaver*), 6.4 (*lapse of options*) and 10 (*corporate events*), unless the Compensation Committee determines otherwise, Options shall Vest in equal tranches of 1/36th at the end of each calendar month following the Date of Grant and may only be exercised after the later of:

(a) the third anniversary of the Date of Grant (the "**Normal Vesting Date**"); and

(b) the date on which any applicable Performance Condition(s) have been satisfied or waived in accordance with Rule 4.2.

Death of an Optionholder

6.2 Save as provided in Rule 6.4 (*lapse of options*), if an Optionholder dies whilst he is employed within the Group or while time is running under Rule 6.3 (*cessation of employment or consultancy as a good leaver*) his personal representatives may exercise his Option at any time within the period of 12 months after the date of his death to the extent it had Vested, and any applicable Performance Condition(s) had been satisfied, at that date.

Cessation of employment or consultancy as a good leaver

6.3 Save as provided in Rule 6. 4 (*lapse of options*), if an Optionholder who is an Employee ceases to be employed within, or an Optionholder who is a Consultant ceases to provide consultancy services to, the Group:

(a) by reason of illness, injury or disability (evidenced to the satisfaction of the Compensation Committee);

(b) in the case of an Employee, by reason of redundancy within the meaning of the Employment Rights Act 1996;

(c) by reason that the only company, undertaking or part-undertaking within the Group by which he is employed or to which he provides consultancy services ceases to be a member of, or is transferred outside, the Group; or

(d) for any other reason which the Compensation Committee considers justifies his treatment as a Good Leaver,

he may exercise his Option within the period of three months after the Cessation Date (or such longer period as the Compensation Committee may decide) to the extent it had Vested, and any applicable Performance Condition(s) had been satisfied, on that Date. For the avoidance of doubt, any portion of his Option that is Unvested as of the Cessation Date shall lapse.

Lapse of options

6.4 Options shall lapse on the earliest of the following events:

(a) the expiry of the period allowed for the satisfaction of any Performance Condition(s) without such Condition(s) being satisfied;

(b) the expiry of the applicable periods in Rule 6.2 (*death of the Optionholder*) and Rule 6.3 (*cessation of employment or consultancy as a good leaver*) but if an Optionholder dies while time is running under Rule 6.3 the Option shall not lapse until the expiry of the period in Rule 6.2;

(c) the Cessation Date of the Optionholder's employment within, or the provision of consultancy services to, the Group for any reason whatsoever (including wrongful or unfair dismissal in the case of an Optionholder who is an Employee) other than those specified in Rule 6.2 (*death of Optionholder*) and Rule 6.3 (*cessation of employment or consultancy as a good leaver*);

(d) save as provided in Rule 11 (*option rollover*), the expiry of the applicable period in Rule 10 (*corporate events*);

(e) the expiry of the applicable period in Rule 11 (*option rollover*);

(f) the date on which the Optionholder becomes bankrupt or does or omits to do anything as a result of which he is deprived of the legal or beneficial ownership of the Option.; and

(g) the tenth anniversary of the Date of Grant (provided that, in the case of an Incentive Stock Option granted to a Ten Percent Owner, such Incentive Stock Option shall lapse on the fifth anniversary of the Date of Grant).

7 MANNER OF EXERCISE

7.1 Provided it would not then be in breach of any applicable restriction (including, without limitation, the U.S. Sarbanes-Oxley Act of 2002), a Vested Option may be exercised in whole or in part by the Optionholder giving a notice of exercise in such manner as the Company may from time to time determine, including electronically. The notice of exercise shall be accompanied by:

(a) a remittance in cleared funds for the aggregate Exercise Price;

(b) irrevocable instructions to a broker to deliver promptly to the Company an amount equal to the aggregate Exercise Price; or

(c) an application for bridging finance to exercise the Option, in such form as the Company may prescribe.

7.2 The Company shall allot or procure the transfer of Shares pursuant to a notice of exercise within 30 days of the date of exercise. Except for any rights determined by reference to a date preceding the date of allotment, any new Shares allotted shall rank pari passu with the other shares of the same class in issue at that date of allotment.

7.3 For so long as the Shares are admitted to trading on Nasdaq or any other investment exchange the Company will apply for admission or listing (as the case may be) of any new Shares issued as soon as is practicable after their allotment.

8 SHARE SETTLEMENT OF OPTION EXERCISE

Notwithstanding any other provision of this Plan, the Company may agree with an Optionholder that he will undertake a share-settled exercise in respect of any Option that is not an Incentive Stock Option held by him whereby, subject to Rule 9 (*tax liabilities*), on exercise of the Option:

(a) no Exercise Price is paid; and

(b) the Optionholder is given free of charge, a number of Shares calculated in accordance with the following formula:

$$S = N \times (MV - EP) \div MV$$

where:

S = the number of Shares to be delivered to the Optionholder, rounded down to the nearest whole Share

N = the total number of Shares in respect of which the Option is being exercised

MV = the Market Value of a Share at the date of exercise

EP= the Option Exercise Price payable per Share.

9 TAX LIABILITIES

9.1 For the purposes of this Rule "**Tax**" means all UK income tax and primary class 1 (employee) and (to the extent the Compensation Committee decides that it shall be borne by the relevant Optionholder), secondary class 1 (employer) National Insurance Contributions, and their equivalent in any other jurisdiction including the U.S., which may properly be borne by Optionholders by reason of the grant, vesting and/or exercise of options or otherwise as a consequence, directly or indirectly, of being an Optionholder.

9.2 Any Group Company or other person which is liable to account for Tax may withhold the appropriate amount of Tax from the Optionholder's remuneration or make such other arrangements as it considers necessary (including the sale of Shares on behalf of an Optionholder) to finance the amounts due. The amount to be withheld may if necessary be estimated provided that if a subsequent adjustment is required it is made as soon as practicable after the amount has been definitively determined.

9.3 With respect to any Optionholder that resides in the U.S., subject to approval by the Compensation Committee, an Optionholder may elect to have the Group Company's required tax withholding obligation satisfied, in whole or in part, by authorising the Group Company to withhold from the Shares to be issued pursuant to an Option a number of shares with an aggregate Market Value (as of the date the withholding is effected) that would satisfy the withholding amount due; provided, however, that the amount withheld does not exceed the maximum statutory tax rate or such lesser amount as is necessary to avoid liability accounting treatment. The Compensation Committee may also require Options to be subject to mandatory share withholding up to the required withholding amount. For purposes of share withholding, the Market Value of withheld shares shall be determined in the same manner as the value of Shares includible in income of the Optionholder. The required tax withholding obligation may also be satisfied, in whole or in part, by an arrangement whereby a certain number of Shares issued pursuant to the Option are immediately sold and proceeds from such sale are remitted to the Group Company in an amount that would satisfy the withholding amount due.

9.4 If the Company or any other person is liable to account for UK secondary Class 1 national insurance contributions ("**Employers' NICs**") in the UK by virtue of the exercise of an Option the Compensation Committee may make it a condition of the exercise of the Option that the Optionholder either:

(a) meets such liability to pay Employers' NICs; or

(b) enters into an election to transfer the liability for Employers' NICs to the Optionholder in a form approved by HMRC,

and enters into such arrangements as may be approved by HMRC in order to ensure that the Employers' NICs liability can be met.

9.5 The Compensation Committee may make it a condition of the exercise of an Option that the Optionholder enters into:

(a) a joint election under section 431 of the UK Income Tax (Earnings and Pensions) Act 2003 to disregard any restrictions for the purposes of any income tax and primary Class 1 national insurance contributions which may arise as the consequence of the exercise of the Option and to disapply section 425 of that Act; or

(b) a similar election in any other jurisdiction.

9.6 If the Compensation Committee so determines, Optionholders may be offered the opportunity to make other funding arrangements satisfactory to the relevant Group Company or other person in relation to the Tax liability.

9.7 By accepting an Option an Optionholder agrees to indemnify any Group Company and any other person against any Tax liability if and to the extent it is not discharged in accordance with this Rule.

10 CORPORATE EVENTS

Change of control

10.1 Save as provided in Rules 8 (*share settlement of option exercise*) and 11 (*option rollover*), if any person (or group of persons acting in concert (as "**acting in concert**" is defined in The City Code on Takeovers and Mergers) obtains Control of the Company as a result of making a general offer to acquire either:

(a) the whole of the issued ordinary share capital of the Company which is made on a condition such that if it is satisfied the person making the offer will have Control of the Company, or

(b) all the shares in the Company which are of the same class as the Plan Shares,

(a "**Change of Control**") all Unvested Options shall lapse unless and to the extent the Compensation Committee determines otherwise and Vested Options may, subject to Rule 10.3 (*squeeze-out and sell-out*) be exercised on the same day as, and immediately prior to, the Change of Control becoming effective or within such period not exceeding 6 months afterwards as the Compensation Committee shall determine, and any Vested Options not exercised within such period shall lapse.

Scheme of arrangement

10.2 Save as provided in Rules 8 (*share settlement of option exercise*) and 11 (*option rollover*), if under section 899 of the Companies Act 2006 the Court sanctions a compromise or arrangement proposed for the purposes of, or in connection with, a scheme for the reconstruction of the Company or its amalgamation with any other company or companies (a "**Scheme of Arrangement**"), all Unvested Options shall lapse unless and to the extent the Compensation Committee determines otherwise and Vested Options may be exercised on the same day as, and immediately prior to, the Court sanctioning the compromise or arrangement or within such period not exceeding 6 months afterwards as the Compensation Committee shall determine.

Squeeze-out and sell-out

10.3 Save as provided in Rules 8 (*share settlement of option exercise*) and 11 (*option rollover*), if any person (or group of persons acting in concert) becomes bound or entitled to acquire shares in the Company under sections 974 to 979 of the Companies Act 2006 ("*squeeze-out*"

and "sell-out") all Unvested Options shall lapse unless and to the extent the Compensation Committee determines otherwise and Vested Options may be exercised at any time when that person remains so bound or entitled.

Winding-up

10.4 If notice is given of a general meeting at which a resolution will be proposed for the voluntary winding-up of the Company (except for the purposes of a Scheme of Arrangement) all Unvested Options shall lapse unless and to the extent the Compensation Committee determines otherwise and Vested Options may be exercised conditionally on the resolution being passed at any time between the notice of the resolution being given and the resolution being passed or defeated.

11 OPTION ROLLOVER

11.1 This Rule applies if there is a Corporate Event and an Optionholder is offered a new option (the "**New Option**") in exchange for the original Option (the "**Old Option**") and the New Option is equivalent to the Old Option. For the purposes of this Rule a New Option is equivalent to an Old Option if:

(a) it is exercisable in the same manner as the Old Option and subject to the provisions of this Plan as they had effect immediately before the exchange;

(b) the total market value of the Shares subject to the Old Option immediately before the exchange equals, as far as is reasonably practicable, the total market value of the shares or securities subject to the New Option immediately after the exchange; and

(c) the total amount payable to exercise the New Option is equal to the total amount payable to exercise the Old Option.

11.2 If there is a Change of Control or Scheme of Arrangement such that Shares are exchanged for shares or securities in another company and the persons who will own the shares in that other company will be the same, or substantially the same, as the persons who owned the Shares immediately before that Change of Control or Scheme of Arrangement and the Optionholder is offered a New Option which is equivalent to the Old Option, the Old Option shall not become exercisable in accordance with whichever is applicable of Rules 10.1 and 10.2 and shall lapse if and to the extent the Optionholder does not accept the offer of the New Option within one month of the offer date.

11.3 Where any New Options are granted pursuant to this Rule, references to "Options" shall be construed as references to the New Options for which they have been exchanged.

11.4 Where any New Options are granted pursuant to this Rule, such exchange shall be done in compliance with the Code with respect to Optionholders that reside in the U.S.

12 VARIATION OF SHARE CAPITAL

12.1 In the event of any variation in the share capital of the Company by way of capitalisation or rights issue, consolidation, subdivision or reduction or otherwise, the number and kind of Shares subject to any Option and the Exercise Price for each of those Shares shall be adjusted in such manner as the Compensation Committee shall determine to be fair and reasonable.

12.2 The Company will take such steps as are considered necessary to notify Optionholders of any adjustments made under this Rule and may call in, endorse, issue or re-issue any certificate as a result of that adjustment.

13 AMENDMENT

13.1 Subject to Rule 13.2, the Compensation Committee may from time to time amend these Rules provided that no amendment to the advantage of Eligible Employees and Optionholders may be made to the provisions relating to:

(a) the persons to whom Options may be granted;

(b) the limit on the number of Shares in respect of which Options may be granted; and

(c) this Rule,

without the prior approval of the Company's shareholders in general meeting except for minor amendments which the Compensation Committee considers necessary or desirable in order to benefit the administration of the Plan, take account of any changes to the applicable legislation in any country or territory or to obtain or maintain favourable tax, exchange control or regulatory treatment for Optionholders or any Group Company. The Compensation Committee are specifically authorized to exercise their discretion to reduce the exercise price of outstanding Options or effect the repricing of such Options through cancellation and re-grants.

13.2 The Compensation Committee may not make any amendment which would abrogate or adversely affect the subsisting rights of Optionholders unless it is made:

(a) with the written consent of the number of Optionholders who hold Options to acquire 75% of the Shares which would be issued or transferred if all Subsisting Options were exercised; or

(b) by a resolution of a meeting of Optionholders passed by not less than 75% of the Optionholders who attend and vote either in person or by proxy.

14 RELATIONSHIP WITH CONTRACT OF EMPLOYMENT OR FOR PROVISION OF CONSULTANCY SERVICES AND EXCLUSION OF LIABILITY

Notwithstanding any other provision of this Plan:

(a) nothing in this Plan or in any Eligible Person's contract of employment or contract for the provision of consultancy serves shall be construed as giving any Eligible Person a right to be granted an Option under this Plan;

(b) an Eligible Employee or Optionholder shall not be entitled, and by accepting an Option granted under this Plan he shall be deemed to have waived any possible entitlement, to any compensation or loss he may suffer as a result of the exercise by the Compensation Committee of any discretion given to them in accordance with these Rules, or the failure by the Compensation Committee to exercise any such discretion, even if such exercise or failure to exercise constitutes a breach of contract by the Company or any other Group Company which employs the Eligible Employee or Optionholder or a breach of any other duty owed by the Company or any other Group Company or gives rise to any other claim whatsoever; and

(c) if an Eligible Person or Optionholder shall cease to be employed within, or to provide consultancy services to, the Group for any reason whatsoever, including (in the case of an Employees) as a result of being wrongfully or unfairly dismissed, he shall not be entitled, and by accepting an Option he shall be deemed to have waived any possible entitlement, to any sum or benefit to compensate him for any loss or curtailment of any right or benefit accrued or in prospect under the Plan, and no such loss or curtailment shall form part of any claim for damages for breach of any contract of employment or for the provision of consultancy services of any Eligible Person or

Optionholder or compensation for unfair or wrongful dismissal or any other claim whatsoever.

15 ADMINISTRATION

15.1 The Plan shall be administered by the Compensation Committee whose decision on all disputes shall be final.

15.2 The Company shall at all times keep available sufficient authorised and unissued shares, or will ensure that sufficient shares will be available, to satisfy the exercise to the full extent still possible all Options which have neither lapsed nor been fully exercised, taking account of any other obligations of the company to issue unissued shares.

15.3 For the purposes of operating the Plan the Company and other relevant Group Companies will collect and process information relating to Eligible Persons and Optionholders in accordance with the privacy notice which is available from the Company's secretary and, in the case of Eligible Persons and Optionholders in the European Union, the EU General Data Protection Regulation of 25 May 2018.

15.4 Any notice or other communication under or in connection with this Plan may be given by the Company either personally or by post and to the company either personally or by post to the secretary. Items sent by post shall be pre-paid and shall be deemed to have been received 72 hours after posting.

15.5 This Plan shall terminate on the tenth anniversary of the date of its adoption or at any earlier time by resolution of the Compensation Committee. Termination of the Plan shall be without prejudice to the subsisting rights of Optionholders and any other relevant persons.

16 THIRD PARTY RIGHTS

A person who is not a party to any Option granted under this Plan shall not have any rights under or in connection with that Option as a result of the Contract (Rights of Third Parties) Act 1999 except where such rights under any provision of the Plan in relation to any Employer Company of the Optionholder which is not a party to the Option.

17 GOVERNING LAW AND JURISDICTION

This Plan is governed by and shall be construed in accordance with the laws of England and Wales and the courts of England and Wales shall have exclusive jurisdiction to hear any claim or dispute arising out of it.

18 TRADING POLICY RESTRICTIONS

Option exercises under the Plan shall be subject to the Company's insider trading policies and procedures, as in effect from time to time.

19 CLAWBACK POLICY

Shares subject to Options under the Plan shall be subject to the Company's clawback policy, as in effect from time to time.

Exhibit 10.12

BICYCLE THERAPEUTICS PLC

[*Name of Director*]
[*Address*]

2019

Dear [*Name of Director*],

Bicycle Therapeutics plc (the "Company") and your role as a director of the Company

As you are aware the articles of association of the Company (the "**Articles**"), at Article 140, contemplates that the Company will indemnify the Company's directors in relation to specific liabilities incurred by them in the performance of their duties. We are taking this opportunity to afford you the direct benefit of this indemnity in the form of a deed for your benefit (this "**Deed**").

1. Interpretation

1.1 In this Deed:

1.1.1 any defined terms (to the extent undefined herein) shall have the meanings given to them in the Articles;

1.1.2 any reference to a statute or statutory provision is a reference to it as amended, extended or re-enacted from time to time;

1.1.3 unless the context otherwise requires, reference to paragraphs are to paragraphs of this Deed;

1.1.4 any words following the terms including, include, in particular, for example or any similar expression shall be construed as illustrative and shall not limit the sense of the words, description, definition, phrase or term preceding those terms; and

1.1.5 other and otherwise are illustrative and shall not limit the sense of the words, description, definition, phrase or term preceding them.

2. Indemnity

2.1 Subject to paragraph 2.2, without prejudice to any indemnity to which you may otherwise be entitled pursuant to Article 140 of the Articles and subject to the terms of this Deed, you shall be indemnified by the Company against all liabilities, costs, charges, expenses, judgments, settlements, compensation and other awards, damages and losses (including all interest, penalties, fines, taxes and legal costs and all other reasonable professional costs and expenses) ("**Liabilities**") arising out of or in connection with any civil, criminal, administrative, investigative or other proceeding ("**Proceedings**") which relate to any act done or omitted or alleged to be done or omitted by you whilst in the course of acting or purporting to act as a director of the Company and/or any Associated Company of the Company (as defined in section 256(b) of the Act for these purposes) or which arises by virtue of you holding or having held such a position ("**Claim**").

2.2 The indemnity in paragraph 2.1 shall not apply to:

2.2.1 the extent prohibited by the Act or otherwise prohibited by law;

2.2.2 any Liability incurred by you:

2.2.2.1 in defending any Proceedings in which you are convicted or judgement is given against you;

2.2.2.2 in defending any Proceedings brought by the Company or any Associated Company of the Company; and

2.2.2.3 in connection with any application under sections 661(3) or (4) or 1157 of the Act which the court refuses to grant you relief on the application;

2.2.3 any Liability incurred by you to the Company or any Associated Company of the Company;

2.2.4 any fine imposed or sum payable by way of a penalty or fine in any criminal proceedings;

2.2.5 any sum payable to a regulatory authority by way of a penalty or fine in respect of your personal non-compliance with any requirement of a regulatory nature (howsoever arising);

2.2.6 any Liability relating to any taxation or national insurance payable by you in connection with your remuneration or other benefits received from the Company or any Associated Company of the Company;

2.2.7 to the extent you are entitled to recover from any other person (including under any policy of insurance) any amount in relation to a Claim, or

2.2.8 any Liability incurred by, or Claim made against, you which the Board reasonably determines arises out of your fraud, willful deceit, willful misconduct, reckless conduct, dishonest or act of bad faith ("**Misconduct**"), save that if a court, tribunal or regulatory authority thereafter finally determines that the relevant Liability or Claim did not arise as a result of your Misconduct, you may, by notice to the Company, request payment of such amount from the Company as the Company would have been liable to pay under this Deed had the Board not made such a determination and the Company shall make a payment to you upon satisfaction of the obligation in paragraph 2.5.

2.3 *Without prejudice and in addition to any indemnity to which you may otherwise be entitled pursuant to Article 140 of the Articles you shall be indemnified by the Company against all Liabilities incurred by you and Claims in connection with the Company's activities as a trustee of an occupational pension scheme (as defined by section 750(5) of the Finance Act 2004) established under a trust provided that no such indemnity shall extend to any Liability arising out of your fraud or dishonesty or the obtaining by you of any personal profit or advantage to which you were not entitled and you shall be entitled to be indemnified for:*

2.3.1 *any fine imposed in any criminal proceedings;*

2.3.2 *any sum payable to a regulatory authority by way of a penalty or fine in respect of non-compliance with any requirement of a regulatory nature howsoever arising; and*

2.3.3 *any Liability incurred by you:*

2.3.3.1 *in defending any Proceedings in which you are convicted or judgement is given against you;*

2.3.3.2 *in defending any Proceedings brought by the Company or any Associated Company of the Company; and*

2.3.3.3 *in connection with any application under sections 661(3) or (4) or 1157 of the Act which the court refuses to grant you relief on the application.*

2.4 References in paragraphs 2.1 and 2.3 to acts or omissions are to acts or omissions made or omitted to be made [*before, on or*] after the date of this Deed, however:

2.4.1 if a company ceases to be an Associated Company of the Company after the date of this Deed, the Company shall only be liable to indemnify you in respect of Liabilities in relation to that company which were incurred before the date on which the company ceased to be an Associated Company of the Company; and

2.4.2 you, as director of any company which becomes an Associated Company of the Company after the date of this Deed, shall be indemnified only in respect of Liabilities incurred after the date on which that company becomes an Associated Company of the Company.

2.5 The Company's obligation to make any payment to you under paragraphs 2.1 and/or 2.3 is conditional upon you having made an application in writing to the Company supported by such documentation and evidence which, in the reasonable opinion of the Board, is satisfactory to prove that:

2.5.1 the Liability suffered or incurred by you and of the date(s) on which it was suffered or incurred and that it falls within the scope of the indemnities given in paragraphs 2.1 and/or 2.3;

2.5.2 any costs and expenses of any third party (including legal costs) which are to be reimbursed by the Company in accordance with in paragraphs 2.1 and/or 2.3 were properly incurred and reasonable in amount,

and where the is satisfied that these conditions have been fulfilled, the Company shall make payment to you within 20 Business Days of receipt of such application.

3. Notification and Conduct

3.1 If you receive any demand relating to a Claim or become aware of any circumstances which might or may be reasonably expected to give rise to the Company being required to indemnity you pursuant to this Deed and before incurring any costs, charges or expenses in respect of any Claim (including securing legal representation), you shall:

3.1.1 as soon as reasonably practicable, give written notice of the circumstances to the Company, as well as any other information which the Company may reasonably request from time to time;

3.1.2 take all reasonable actions to mitigate any Liability you suffer in respect of the circumstances giving rise to the Claim (including any action that the Company may reasonably request to avoid, dispute, resist, appeal or defend any Claim and shall not make any admission of liability, agreement or compromise with any person in relation to any Claim without the prior written consent of the Company);

3.1.3 forward all documents you receive in respect of such Claim to the Company as soon as reasonably practical following receipt;

3.1.4 assist the Company as it may reasonable require in resisting, defending or settling the Claim; and

3.1.5 provide to the Company all such information in relation to any Claim or Liabilities as the Company may reasonably request, and shall take all such action as the Company may reasonably request.

3.2 The Company or an Associated Company of the Company (as the case may be) will be entitled to take over, negotiate and conduct in the your name the defence to or settlement of any Claim or to prosecute in your name for its own behalf any proceedings relating to a Claim.

3.3 If the Company or an Associated Company of the Company exercises its right pursuant to paragraph 3.2, the Company or relevant Associated Company of the Company shall:

3.3.1 consult with you in relation to the conduct of the Claim or Proceedings on aspects of the Claim or Proceedings materially relevant to you and keep you reasonably information of material developments in the Claim or Proceedings, provided that the Company or Associated Company of the Company shall be under no obligation to provide any information the provision of which is reasonably likely to adversely affect the ability of the Company or an Associated Company of the Company to claim in respect of the relevant loss under any applicable policy of insurance;

3.3.2 take into account the your reasonable requests relating to the Claim or proceedings (including any settlement) on issues which may be reasonably likely to result in material damage to your reputation; and

3.3.3 have full discretion in the conduct or settlement of the Claim or proceedings relating to such Claim provided you are not required to make any contribution to the settlement and the settlement contains no admission of liability by you.

3.4 The Company's obligations owed to you under this Deed (including the obligation to indemnify you in paragraphs 2.1 and 2.3) are conditional upon your compliance with the provisions of this paragraph 3.

4. Miscellaneous

4.1 *Effect of Ceasing to be a Director of the Company or any Associated Company of the Company*

In the event that you cease to be a director of the Company or any Associated Company of the Company, this Deed shall remain in force and you will continue to be indemnified in accordance with the terms and conditions of this Deed, until such time as any relevant limitation periods for bringing Claims against you have expired, or for so long as you remain liable for any Liabilities, notwithstanding that you may have ceased to be a director of the Company or any Associated Company of the Company.

4.2 *Subrogation*

The Company shall, in the event that a payment is made to you under this Deed in respect of a particular Liability, be entitled to recover from you an amount equal to any payment received by you under any policy of insurance or from any other third party source to the extent that such payment relates to the Liability, or if the payment received by you is greater than the payment made under this Deed, a sum equal to the payment made under this Deed. You shall pay over such sum promptly on the Company's request.

4.3 *No Double Recovery*

You shall not be entitled to recover any Liability more than once and in the event that the Company makes payment under this Deed, the Company shall be subrogated to the extent of such payment to all of your rights of recovery against third parties (including nay claim under any applicable directors' and officer's insurance policy) in respect of the payment and you shall do everything that may be necessary to secure any such rights including:

4.3.1 the execution of any documents necessary to enable the Company effectively to bring an action in your name; and

4.3.2 the provision of assistance as a witness.

4.4 *Assignment*

The Company may at any time assign, mortgage, charge, subcontract, delegate, declare a trust over or deal in any other manner with any or all of its rights under this Deed, provided that it gives notice of such dealing to you. You shall not assign, transfer, mortgage, charge, subcontract, declare a trust over or deal in any other manner with any of your rights and obligations under this Deed.

4.5 *Entire Agreement*

This Deed constitutes the entire agreement between the parties and supersedes and extinguishes all previous agreements, promises, assurances, warranties, representations and understandings between them, whether written or oral, relating to its subject matter.

4.6 *Severance*

If any provision or part-provision of this Deed is or becomes invalid, illegal or unenforceable, it shall be deemed modified to the minimum extent necessary to make it valid, legal and enforceable. If such modification is not possible, the relevant provision or part-provision shall be deemed deleted. Any modification to or deletion of a provision or part-provision under this paragraph 4.5 shall not affect the validity and enforceability of the rest of this Deed. If one party gives notice to the other of the possibility that any provision or part-provision of this Deed is invalid, illegal or unenforceable, the parties shall negotiate in good faith to amend such provision so that, as amended, it is legal, valid and enforceable, and, to the greatest extent possible, achieves the intended commercial result of the original provision.

4.7 *Notices and Demands*

4.7.1 Any notice or demand given to a party under or in connection with this Deed shall be:

4.7.1.1 in writing and in English;

4.7.1.2 shall be signed by or on behalf of the party giving it;

4.7.1.3 shall be sent by a method listed in paragraph 4.7.2;

4.7.1.4 is deemed received as set out in paragraph 4.7.2 if prepared and sent in accordance with this paragraph.

4.7.2 This paragraph 4.7.2 sets out the delivery methods for sending a notice to a party under this Deed and, for each delivery method, the date and time when the notice is deemed to have been received (provided that all other requirements of this paragraph have been satisfied and subject to the provisions in paragraph 4.7.3:

(a) if delivered by hand, on signature of a delivery receipt or at the time the notice is left at the address;

(b) if sent by pre-paid first class post or other next working day delivery service, at the time recorded by the delivery service;

(c) if sent by pre-paid airmail, at the time recorded by the delivery service;

(d) if sent by email, at the time of transmission; or

(e) if sent by document exchange ("**DX**"), at 9.00 am on the Business Day after being put into the DX.

4.7.3 If deemed receipt under paragraph 4.7.2 would occur outside business hours in the place of receipt, it shall be deferred until business hours resume. In this paragraph, business hours means 9.00am to 5.00pm Monday to Friday on a day that is not a public holiday in the place of receipt.

4.7.4 This paragraph 4.7 does not apply to the service of any proceedings or other documents in any legal action or, where applicable, any arbitration or other method of dispute resolution.

4.8 *Variation*

4.8.1 No variation of this Deed shall be effective unless it is in writing and signed by the parties (or their authorised representatives).

4.8.2 No failure or delay by a party to exercise any right or remedy provided under this Deed or by law shall constitute a waiver of that or any other right or remedy, nor shall it prevent or restrict the further exercise of that or any other right or remedy. No single or partial exercise of such right or remedy shall prevent or restrict the further exercise of that or any other right or remedy.

4.9 *Counterparts*

4.9.1 This Deed may be executed in any number of counterparts, each of which when executed and delivered shall constitute a duplicate original, but all the counterparts shall together constitute the one deed.

4.9.2 Transmission of an executed counterpart of this Deed (but for the avoidance of doubt not just a signature page) by email (in PDF, JPEG or other agreed format),shall take effect as delivery of an executed counterpart of this Deed.

4.9.3 No counterpart shall be effective until each party has executed and delivered at least one counterpart.

4.10 *Third Party Rights*

Unless this Deed expressly states otherwise, this Deed does not confer any rights on any person or party (other than the parties to this Deed and any Associated Company of the Company) pursuant to the Contracts (Rights of Third Parties) Act 1999.

4.11 *Governing Law and Jurisdiction*

4.11.1 This Deed and any dispute or claim arising out of or in connection with its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

4.11.2 You and the Company irrevocably agree that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim that arises out of or in connection with this Deed or its subject matter or formation (including non-contractual disputes or claims).

[*Deliberately left blank, signature page to follow.***]**

IN WITNESS WHEREOF, this Deed has been executed as a deed by the Company and you, or such parties' duly authorised attorneys on the day and year first above written.

EXECUTED as a **DEED** and delivered by)
for and on behalf of)
BICYCLE THERAPEUTICS PLC) _____

In the presence of:

Witness signature: _____

Name: _____

Address: _____

_____

_____

Occupation: _____

EXECUTED as a **DEED** and delivered by)
[***Name of Director or Officer***])
) _____

In the presence of:

Witness signature: _____

Name: _____

Address: _____

_____

_____

Occupation: _____

Exhibit 10.13

DATE: 2 March 2017

UNDERLEASE OF GROUND AND FIRST FLOOR PREMISES BUILDING 900
BABRAHAM RESEARCH CAMPUS BABRAHAM CAMBRIDGE

Between

(1) IMPERIAL COLLEGE THINKSPACE LIMITED

and

(2) CONVERGENCE PHARMACEUTICALS LIMITED

and

(3) BIOGEN IDEC LIMITED

CMS Cameron McKenna LLP
Cannon Place
78 Cannon Street
London EC4A 6AF
T +44 20 7367 3000
F +44 20 7367 2000
Reference: KTBR/MRH/101433.00238

Table of Contents

LAND REGISTRY PRESCRIBED CLAUSES

LR1. Date of lease

2 March 2017

LR2. Title number(s)

LR2.1 Landlord's title number(s)
Title number(s) out of which this lease is granted. Leave blank if not registered.

CB406367

LR2.2 Other title numbers
Existing title number(s) against which entries of matters referred to in LR9, LR10, LR11 and LRI3 are to be made.

CB303470

LR3. Parties to this lease

Landlord

IMPERIAL COLLEGE THINKSPACE LIMITED having its registered office at Faculty Building, Level 1, Imperial College, London SW7 2AZ (company registration number 05272659)

Tenant

CONVERGENCE PHARMACEUTICALS LIMITED (a Biogen company) (registered number 09376285) having its registered office at 70 Norden Road, Maidenhead, Berkshire, SL6 4AY

Other parties

Surety

BIOGEN IDEC LIMITED (registered number 01497267) having its registered office at Innovation House, 70 Norden Road, Maidenhead, Berkshire, SL6 4AY

LR4. Property

In the case of a conflict between this clause and the remainder of this lease then, for the purposes of registration, this clause shall prevail.

The premises described in part 1 of schedule 1

LR5. Prescribed statements etc.

LR5.1 Statements prescribed under rules 179 (dispositions in favour of a charity), 180 (dispositions by a charity) or 196 (leases under the Leasehold Reform, Housing and Urban Development Act 1993) of the Land Registration Rules 2003.

None

	LR5.2 This lease is made under, or by reference to, provisions of:
LR6. Term for which the Property is leased	The term is as follows: 5 years from and including 12 December 2016
LR7. Premium	None
LR8. Prohibitions or restrictions on disposing of this lease	This lease contains a provision that prohibits or restricts dispositions.
LR9. Rights of acquisition etc.	**LR9.1 Tenant's contractual rights to renew this lease, to acquire the reversion or another lease of the Property, or to acquire an interest in other land** None **LR9.2 Tenant's covenant to (or offer to) surrender this lease** None **LR9.3 Landlord's contractual rights to acquire this lease** None
LR10. Restrictive covenants given in this lease by the Landlord in respect of land other than the Property	None
LR11. Easements	**LR11.1 Easements granted by this lease for the benefit of the Property** See part 2 of schedule 1 **LR11.2 Easements granted or reserved by this lease over the Property for the benefit of other property** See part 3 of schedule 1

LR12. Estate rentcharge burdening the Property	None
LR13. Application for standard form of restriction	None
LR14. Declaration of trust where there is more than one person comprising the Tenant	None

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THIS UNDERLEASE dated and made between the parties as specified in the Land Registry Prescribed Clauses

WITNESSES AS FOLLOWS:-

1. Definitions and interpretation

In this Underlease unless the context otherwise requires:-

1.1 the words defined in this sub-clause have the following meanings:-

"1954 Act": the Landlord and Tenant Act 1954

"1995 Act": the Landlord and Tenant (Covenants) Act 1995

"2003 Order": the Regulatory Reform (Business Tenancies) (England and Wales) Order 2003

"Asset Rating": has the meaning given in the EPB Regulations

"Building": the land and the building known as Building 900, Babraham Research Campus, Babraham Cambridge comprised in title number CB406367 shown edged in red on Plan A

"Common Media": all Service Media serving the Premises and other parts of the Building

"Common Parts": the car parking areas roads paths landscaped areas entrance halls reception areas lifts fire escapes staircases passages and landings and toilets and showers of the Building and any other areas or amenities that are used or enjoyed in common by some or all of the tenants or occupiers of the Building

"CRC": the Carbon Reduction Commitment Energy Efficiency Scheme as defined in section 3 of the CRC Energy Efficiency Scheme Order 2013 or any similar scheme amending or replacing it

"DEC": a Display Energy Certificate and Advisory Report as defined in the EPB Regulations

"EPB Regulations": the Energy Performance of Buildings (Certificates and Inspections) (England and Wales) Regulations 2007

"EPC": an Energy Performance Certificate and Recommendation Report as defined in the EPB Regulations

"Estate Service Charge": the fair proportion properly attributable to the Premises of the sums payable by the Landlord pursuant to paragraph 7 of schedule 2 to the Superior Lease as determined from time to time by the Landlord's surveyor acting

fairly and reasonably and to be based on the proportion that the net internal area of the Premises bears to the total net internal area of the Lettable Premises

"Ethos": has the meaning ascribed to that expression in the Superior Lease

"Expiry of the Term": the date of the expiration (but not of any sooner determination) of the Term.

"Group Company": a company which is a Subsidiary or Holding Company of the Tenant or any Subsidiary of such Holding Company from time to time (and for this purpose **"Subsidiary"** and **"Holding Company"** have the meanings given in section 1159 and Schedule 6 of the Companies Act 2006) or a company in which a person has a controlling interest where the same person also holds a controlling interest in the Tenant and for this purpose a person has a controlling interest if (had that person been a company) the other company and the Tenant would each have been its Subsidiary

"Heating Systems": the pipes ducting boilers and other installations for the provision in the Building of hot water heating and cooling and ventilation

"Inherent Defect": any defect in the structure of the Premises or the Building or the Service Media within the Building which is attributable to defective design, workmanship or materials in its original construction the defective supervision of the construction of or the defective installation of anything in or on the Premises or the Building (as part of its original construction) or the defective preparation of the site on which the Premises or the Building are constructed and such defect existed but would not have been apparent on inspection of the Premises or the Building by an appropriate competent professional person at the date of this Lease

"Initial Service Charge": seventy nine thousand three hundred and seven pounds and six pence (€79,307.06) per annum

"Insurance Rent": the yearly sum (and proportionately for any period less than a year) equal to the due proportion attributable to the Premises (which proportion shall be determined from time to time by the Landlord's surveyor acting fairly and reasonably) of the gross amounts expended by the Landlord from time to time in insuring the Building against the Insured Risks pursuant to the Superior Lease together with insurance for not less than three years' loss of rent and against liabilities of the Landlord in respect of property owner's and third party risks and the cost of any insurance valuations of the Building carried out by or on behalf of the Landlord not more often than once in every year

"Insured Risks": such risks as may be insured against by the Landlord from time to time under the provisions of the Superior Lease

"Insurers": such reputable insurers as the Landlord may nominate from time to time

"Interest Rate": whichever shall be the higher of 1% per annum and the percentage rate per annum equal to the base lending rate from time to time of Lloyds TSB Bank plc (or another bank nominated from time to time by the Landlord) or (if base lending

rates cease to be published) such other equivalent rate of interest specified by the Landlord (acting reasonably)

"Landlord": the landlord referred to in clause LR3 and the person from time to time entitled to the reversion immediately expectant on the termination of the Term

"Landlord's Expenses": reasonable and proper solicitors' counsels' surveyors' and other consultants' and professional fees and costs bailiffs' fees and management charges incurred by the Landlord

"Lettable Premises": accommodation within the Building from time to time let or occupied or intended for letting or occupation

"Operational Rating": has the meaning given in the EPB Regulations

"Permitted Use": laboratories with ancillary offices and meeting rooms for research and development activities for the purposes of scientific and/or medical research in connection with human health care or biotechnology

"Plan": a plan attached to this deed and references to a lettered or numbered plan are to the plan so lettered or numbered

"Planning Acts": the Town and Country Planning Act 1990 the Planning (Listed Buildings and Conservation Areas) Act 1990 the Planning (Hazardous Substances) Act 1990 the Planning (Consequential Provisions) Act 1990 the Planning and Compensation Act 1991 the Planning and Compulsory Purchase Act 2004 and all other statutes regulating the development design use and control of property

"Premises: the Property referred to in clause LR4

"Quarter Days": 25th March 24th June 29th September and 25th December in each year

"Rent": three hundred and forty nine thousand eight hundred and eighty four pounds and nine pence (€349,884.09) per annum

"Rent Commencement Date": 10 April 2017

"Rents": the Rent the Insurance Rent the Service Charge the Estate Service Charge and the other sums reserved by or payable by the Tenant under this Underlease

"Retained Premises": the Building excluding the Premises and any other Lettable Premises

"Service Charge": has the meaning given to such expression in part 1 of schedule **8**

"Service Charge Commencement Date": the first day of the Term

"Service Media": all sewers drains pipes gullies gutters ducts mains channels wires cables conduits flues and other conducting media

"Service Risers": the service risers shown edged in yellow on Plans B and C

"Superior Lease": a lease dated 12 August 2015 made between Biotechnology and Biological Sciences Research Council (1) Imperial Bioincubator Limited (2) and Imperial College of Science Technology and Medicine (3) and any document which is supplemental to or collateral with or entered into pursuant to such lease

"Superior Lessor": includes the person from time to time entitled to the reversion immediately or mediately expectant on the determination of the term granted by the Superior Lease

"Surety": the surety referred to in clause LR3 or if none is referred to Surety means any surety or sureties of the Tenant's obligations under this Underlease from time to time and where the Surety is an individual includes the Surety's personal representatives

"Tenant": the tenant referred to in clause LR3 or the person who is from time to time the tenant under this Lease

"Term": the term as set out in clause LR6

"this Underlease": this deed as varied from time to time and any document which is supplemental to or collateral with or entered into pursuant to this deed

"Toilets and Showers": the toilets and showers on the ground and first floors of the Building forming part of the common areas shown coloured green and marked "GIO2 Toilets and Showers" and "F102 Toilets and Showers" on Plans B and C respectively

"Unit B External Store": the external store shown edged and shaded blue on Plan B and marked "BSO1 Bin Store", "BSO2 General Store" and "BS03 Gas Store"

"Value Added Tax": value added tax and any tax or duty of a similar nature

"Wireless Data Services": equipment or systems providing or related to wireless data voice or video connectivity or wireless services permitting or offering access to the internet or any wireless network mobile network or telecommunications system which involves a wireless or mobile device

1.2 any covenant given by more than one person will be joint and several

1.3 where there are two or more persons at any time included in the expressions **"Landlord"** and/or **"Tenant"** and/or **"Surety"** references to the **"Landlord"** and/or the **"Tenant"** and/or the **"Surety"** will include all or any one of them

1.4 references to any statute statutory provision directive of the Council of the European Union (whether issued jointly with any other person or under any other name) or other legislation include a reference to that statute statutory provision directive or legislation as amended extended re-enacted consolidated or replaced from time to time (whether before or after the date of this Underlease) and include any order regulation instrument or other subordinate legislation made under the relevant statute statutory provision

directive or legislation (except in the case of any reference to the Town and Country Planning (Use Classes) Order 1987)

1.5 every obligation of any party to this Underlease not to do an act or thing includes an obligation not to allow it to be done

1.6 where there is an obligation to obtain the consent or approval of the Landlord under this Underlease such consent or approval must be in writing and such obligation includes where necessary an obligation to obtain the consent or approval in writing of the Superior Lessor and/or any chargee from time to time

1.7 any reference to consent or approval not being unreasonably withheld also means it must not be unreasonably delayed

1.8 any consent or approval must be obtained before the act or event to which it applies is carried out or done and will be effective only if in the form the party giving it properly requires

1.9 where the Landlord has a right to enter the Premises such right will also be exercisable by the Landlord's agents any chargee or superior landlord from time to time and all persons authorised by them with or without workmen and equipment

1.10 any reference to the end of the Term means the expiration or earlier termination of this Underlease for whatever reason

1.11 words denoting persons include firms companies and corporations and vice versa

1.12 the singular includes the plural and vice versa and one gender includes any other

1.13 any reference to the Landlord's surveyor includes any surveyor employed by the Landlord or by any company associated with the Landlord

1.14 references to clauses paragraphs and schedules are to clauses and paragraphs of and schedules to this deed

1.15 the headings to clauses paragraphs and schedules do not affect the construction of this Underlease

1.16 the words **"include" "includes"** and **"including"** are deemed to be followed by the words **"without limitation"**

1.17 references to any act or omission of the Tenant extend to any act or omission of any sub-tenant or licensee of the Tenant or any person at the Premises or the Building with the consent of the Tenant any sub-tenant or any licensee

2. Demise and reddendum

The Landlord demises the Premises to the Tenant with full title guarantee TOGETHER WITH (in common with all other persons from time to time entitled to them) the rights mentioned in part 2 of schedule 1 EXCEPT AND RESERVING to the Landlord and all other persons from time to time entitled to them the rights mentioned

in part 3 of schedule 1 TO HOLD for the Term SUBJECT to and with the benefit of the provisions contained or referred to in any documents specified and the matters referred to in schedule 6 and any easements rights and privileges enjoyed by any other land or person which affect the Premises YIELDING AND PAYING for them:-

2.1 the Rent by equal quarterly payments in advance on the Quarter Days and proportionately for any period less than a year the first payment (being the proportion for the period from and including the Rent Commencement Date to and including the day before the next following Quarter Day) to be made on the Rent Commencement Date and

2.2 as additional rents:-

2.2.1 within 14 days of written demand the Insurance Rent

2.2.2 the Service Charge in accordance with Schedule 9

2.2.3 within 14 days of written demand (with appropriate evidence) the Estate Service Charge

2.2.4 any Value Added Tax from time to time payable by the Tenant under this Underlease and

2.2.5 within 14 days of written demand all other sums payable or repayable by the Tenant to the Landlord under this Underlease

3. Tenant's covenants

The Tenant COVENANTS with the Landlord to observe and perform the obligations of the Tenant contained in schedule 2 (Tenant's covenants) schedule 5 (Insurance) and schedule 8 (Services and the Service Charge) or otherwise arising under this Underlease

4. Landlord's covenants

The Landlord COVENANTS with the Tenant to observe and perform the obligations of the Landlord contained in schedule 3 (Landlord's covenants) schedule 5 (Insurance) and schedule 8 (Services and the Service Charge) or otherwise arising under this Underlease

5. Provisos

PROVIDED ALWAYS and it is agreed and declared as set out in schedule 4 (Provisos)

6. Surety covenants

The Surety COVENANTS with the Landlord in the terms set out in schedule 7 (Covenants by Surety)

7. Exclusion of sections 24 - 28 of the 1954 Act

7.1 The Tenant confirms that before it became contractually bound to enter into the tenancy created by this deed:-

7.1.1 the Landlord served a notice dated 8 June 2016 (the **"Notice"**) on the Tenant in accordance with section 38A(3)(a) of the 1954 Act

7.1.2 the Tenant (or a person duly authorised by the Tenant) made a statutory declaration dated 9 June 2016 (the **"Declaration"**) confirming receipt of the Notice in accordance with schedule 2 to the 2003 Order

7.2 The Tenant further confirms that where the Declaration was made by a person other than the Tenant that person was duly authorised by the Tenant to make the Declaration on the Tenant's behalf

7.3 The parties agree that sections 24 to 28 (inclusive) of the 1954 Act will not apply to the tenancy created by this deed

8. Tenant's option to renew

8.1 If the Tenant wishes to enter into a further lease of the Premises for a term of five years commencing on and including the 12th day of December 2021 upon the same terms and conditions as this Lease (including the exclusion of sections 24 to 28 (inclusive) of the 1954 Act in accordance with section 38A of the 1954 Act) except as varied by the provisions of Schedule 9 (the **"Further Lease"**) the Tenant must first serve written notice on the Landlord indicating such intention (the **"Intention Notice"**) not more than twelve nor less than eight months before the Expiry of the Term

8.2 Within twenty eight days of receipt of the Intention Notice the Landlord will serve notice on the Tenant in relation to the tenancy to be granted by the Further Lease in accordance with section 38A(3)(a) of the 1954 Act

8.3 When:-

8.3.1 the Landlord has served notice on the Tenant in accordance with clause 8.2 and

8.3.2 the Tenant has made the appropriate declaration or statutory declaration confirming receipt of such notice in accordance with schedule 2 to the 2003 Order (as required to give effect to the agreement by the Landlord and the Tenant to exclude the provisions of sections 24 to 28 (inclusive) of the 1954 Act to be contained in the Further Lease in accordance with the provisions of section 38A of the 1954 Act)

then the Tenant may elect to take the Further Lease by written notice to that effect (the **"Option Notice"**) to the Landlord not less than six months before the Expiry of the Term PROVIDED ALWAYS that if having served an Intention Notice the Tenant does not serve the Option Notice for any reason the Tenant will pay to the Landlord on demand on an indemnity basis all costs and expenses (including all Landlord's Expenses) incurred by the Landlord in relation to the Intention Notice and the performance of its obligations under this clause 8

8.4 the Landlord and the Tenant agree to use all reasonable endeavours to procure the satisfaction of the conditions contained in clauses 8.2 and 8.3

8.5 Subject always to the provisions of clause 8.6 the Option Notice will not be binding on the Landlord unless it:-

8.5.1 recites the agreement of the Landlord and the Tenant that sections 24 to 28 (inclusive) of the 1954 Act will not apply to the tenancy to be created by the Further Lease and

8.5.2 contains confirmation by the Tenant that before the date of the Option Notice:-

(a) the Landlord served a notice (the **"Notice")** on the Tenant in accordance with section 38A(3)(a) of the 1954 Act

(b) the Tenant (or a person duly authorised by the Tenant) made a declaration or statutory declaration (the **"Declaration")** confirming receipt of the Notice in accordance with schedule 2 to the 2003 Order and

(c) that where the Declaration was made by a person other than the Tenant that person was duly authorised by the Tenant to make the Declaration on the Tenant's behalf

8.6 PROVIDED:-

8.6.1 the Option Notice has been validly served in accordance with the provisions of clause 8.3 and complies in all respects with the provisions of clause 8.5

8.6.2 the Tenant has paid all costs and expenses (including all Landlord's Expenses) incurred by the Landlord in relation to the grant of the Further Lease and the performance of its obligations under this clause 8 and

8.6.3 any surety of the Tenant's obligations under this Lease joins in the Further Lease to covenant with the Landlord in the terms contained in schedule 7 (mutatis mutandis)

the Landlord will grant and the Tenant will take the Further Lease of the Premises on or (if earlier) not more than one month before the Expiry of the Term PROVIDED FURTHER that where either the Tenant and/or any surety of the Tenant's obligations under the Further Lease are incorporated under the laws of any jurisdiction other than England and Wales they have also in each case provided immediately prior to such grant a legal opinion (addressed to and in a form reasonably acceptable to the Landlord on the advice of the Landlord's solicitors and dated not more than 14 days prior to such grant) prepared by legal advisers duly qualified to practice in the relevant jurisdiction confirming (i) the validity of the execution of the Further Lease by the Tenant and/or any such surety and (ii) the enforceability of the Further Lease under the laws of the relevant jurisdiction

8.7 At any time after the Expiry of the Term a party who is ready able and willing to complete the grant of the Further Lease may serve on the other a notice to complete the grant of the Further Lease in accordance with this clause 8 (**"Completion Notice"**) and in connection with the service of any Completion Notice:

8.7.1 a party is ready able and willing to complete if it could be but for the default of the other party

8.7.2 the parties are to complete the grant of the Further Lease within fourteen days of serving a Completion Notice (excluding the date on which the Completion Notice is served) as to which time shall be of the essence

8.7.3 if either party receives but fails to complete the grant of the Lease in accordance with a Completion Notice that has been validly served under this clause 8 this option will be terminated but without prejudice to any other right or remedy of either party against the other

8.8 This option will be of no effect unless registered at HM Land Registry as appropriate within three months from the date of this Lease

IN WITNESS of which the parties have executed this Underlease as a deed and have delivered it upon dating it

Schedule 1

Part 1

The Premises

1. The premises shown edged and shaded in blue on Plans B and C comprising parts of the ground and first floors of the Building but excluding the Service Risers and the Unit B External Store

2. The Premises include all additions alterations and improvements to them and also include: -

2.1 the plaster and decorative finishes applied to the interior of the external walls of the Building and to any structural or load-bearing walls and columns within the Premises but no other part of any such walls and columns

2.2 the whole of any non-structural or non-load-bearing walls and columns within the Premises

2.3 the inner half severed medially of any non-structural or non-load-bearing walls dividing the Premises from other parts of the Building

2.4 the doors door furniture and door frames of or within the Premises

2.7 the windows and window frames of or within the Premises but not any windows window frames or any forms of glazing which are in or comprise part of the external walls of the Building

2.8 all Service Media (other than the Heating Systems) vested in the Landlord which exclusively serve the Premises up to the point where they connect to those of statutory undertakers or to those which are Common Media

Part 2

Rights granted

1. A right to the free and uninterrupted passage and running of all services from and to the Premises through all Common Media including (without limitation via the Services Risers)

2. A right (subject to paragraph 28 of schedule 2) to use the Common Parts for the purposes properly applicable to them

3. A right to park private motor cars in the car parking areas forming part of the Common Parts on a first-come first-served basis

4. A right to use the Toilets and Showers

5. A right to use the bicycle racks in the bicycle storage area shown edged in green on Plan D and forming part of the Building

6. A right to enter (at reasonable times and after giving reasonable written notice):-

6.1 such other parts of the Building as may reasonably be necessary for the purpose of carrying out any cleaning of or repairs (here including installing in positions previously approved by the Landlord (acting reasonably) or replacing where necessary) to any Service Media forming part of the Premises or any air conditioning or other equipment installed by the Tenant under the terms of this Lease and the lift to be installed by the Tenant in the Common Parts or otherwise complying with the Tenant's obligations under this Underlease the Tenant doing as little damage as possible and making good all physical damage caused to the Building to the reasonable satisfaction of the Landlord and complying with the reasonable requirements of and causing the minimum of inconvenience to the occupiers of such other parts of the Building

6.2 such other parts of the Building as may be reasonably necessary for the purposes of carrying out repairs or permitted alterations where not otherwise practicable to the Premises the Tenant doing as little damage as possible and making good all physical damage caused to the Building to the reasonable satisfaction of the Landlord and complying with the reasonable requirements of and causing the minimum of inconvenience to the occupiers of such other parts of the Building

6.3 such parts of the Common Parts as may reasonably be necessary to carry out any assessment or inspection necessary to prepare an EPC the Tenant doing as little damage as possible and making good all physical damage caused to the Common Parts to the reasonable satisfaction of the Landlord and causing the minimum of inconvenience to the other occupiers of the Building

7. A right of support and shelter for the Premises from other parts of the Building

8. A right to erect in such part of the entrance hall of the Building as the Landlord may nominate a sign indicating the name and business of the Tenant

9. A right to include the Tenant's name on directional signage at the entrance to Babraham Research Campus and on directional signage within the Campus where the same has been erected by the Landlord with the consent of the Superior Landlord pursuant to the Superior Lease

10. A right to use reception services at the reception in the main entrance to the Building where the same are made available to all occupiers of the Building

11. The rights specified in clause 3.2 of the Superior Lease

12. The exclusive right to use the Unit B External Store for the storage of hazardous waste and other materials subject to compliance with the reasonable requirements of the Landlord notified to the Tenant from time to time

Part 3

Rights excepted and reserved

1. A right to enter the Premises on giving to the Tenant not less than 48 hours prior written notice (except in an emergency) to inspect the state and condition of the Premises to determine whether the Tenant is complying with its obligations in this Underlease and to take any action to remedy any breach of such obligations

2. A right to enter the Premises on giving to the Tenant not less than 48 hours prior written notice (except in an emergency) and at reasonable times (the persons exercising such right causing as little damage as possible and complying with the reasonable requirements of and causing the minimum of inconvenience to the occupiers of the Premises and making good any physical damage caused to the Premises by the exercise of such right to the reasonable satisfaction of the Tenant) for the following purposes:-

2.1 to erect and retain scaffolding outside the Building bordering onto the Premises for constructing altering repairing or cleaning any other land in which the Landlord may from time to time have any interest notwithstanding any temporary restriction of the use and enjoyment of the Premises by the Tenant

2.2 to erect and retain masts satellite dishes and antennae on the external walls and the roof of any building forming part of the Premises

2.3 to inspect maintain clean repair alter test renew or replace any other land buildings premises or Service Media and to lay and make connections to any Service Media within but not exclusively serving the Premises

2.4 to carry out any assessment or inspection necessary to prepare an EPC

2.5 to comply with any of the covenants on the part of the Landlord or the conditions contained in or preventing a forfeiture of the Superior Lease (notwithstanding that the obligation to comply with such covenants and conditions is imposed on the Tenant by this Underlease)

2.6 to gain access to the Service Risers

2.7 for any other proper purpose mentioned in this Underlease or for any other reasonable or proper purpose connected with the Landlord's interest in the Building

and the Landlord shall comply with paragraph 5 of schedule 3 in exercising the rights of entry reserved by paragraphs 1 and 2 above

3. A right to the free and uninterrupted passage and running of all services from and to all other parts of the Building and all other buildings and land through and along all Service Media from time to time within the Premises but which do not exclusively serve the Premises

4. All rights of light or air now subsisting or which might (but for this exception) be acquired over any other land

5. A right to build upon and to maintain repair replace and renew any other part or parts of the Building and any adjoining land or buildings of the Landlord in such manner as the Landlord may think fit without compensation to the Tenant PROVIDED THAT reasonable means of access to the Premises are available at all times and that the Tenant's use and enjoyment of the Premises are not materially adversely affected

6. A right of support and shelter from the Premises for the remainder of the Building

7. The rights reserved by clauses 4.1 and 4.2 of the Superior Lease

Schedule 2

Tenant's covenants

1. Pay Rents and interest

1.1 To pay the Rents without deduction counterclaim or set off (whether in each case legal or equitable) at the stated times in cleared funds (and if the Landlord so requires by banker's standing order or automated credit)

1.2 Without prejudice to any other right remedy or power of the Landlord if any of the Rents are not paid on the due dates to pay on demand to the Landlord interest on them at three per cent per annum above the Interest Rate (before and after any judgement) from the date when they became due until payment calculated on a daily basis

2. Pay taxes outgoings and for utility services

2.1 To pay all rates taxes charges and other sums or outgoings (whether or not of a capital or non-recurring nature) which are payable or may be charged or assessed on the Premises or on the owner or occupier of them (excluding any payable by the Landlord in respect of the receipt of Rents or relating to any dealing with the reversion to this Underlease) and in the absence of direct assessment to pay to the Landlord a fair proportion of them (to be determined by the Landlord acting reasonably) and to the extent that the Landlord may be liable to make payments and/or incurs costs in complying with CRC in respect of the Building then subject to the Landlord providing to the Tenant details of the costs incurred and the proposed apportionment of such costs a fair proportion of the same (to be determined by the Landlord acting reasonably)

2.2 To pay the suppliers for and indemnify the Landlord against all charges for gas water drainage electricity telephone and any other services to the Premises which are separately metered and to pay all equipment rents and in the absence of direct assessment to pay a fair proportion of them (to be determined by the Landlord acting reasonably)

3. Repair

To keep the Premises in good and substantial repair and condition (damage by any Insured Risk excepted save to the extent that the insurance money is irrecoverable by reason of the act or default of the Tenant) and these obligations include the following:-

3.1 where necessary and also in the six months before the end of the Term to decorate the Premises (in the six months before the end of the Term in such colours as the Landlord may reasonably require)

3.2 to keep the Premises clean and tidy and to clean the inside of the windows regularly

3.3 to maintain regularly and when necessary repair or replace all gas electrical hydraulic and other mechanical installations and equipment (if any) forming part of and exclusively serving the Premises to the reasonable satisfaction of the Landlord

3.4 to carry out all works of repair decoration and maintenance and other treatment of the Premises in a proper and workmanlike manner in accordance with good practice current at the time and with good quality suitable and sufficient materials and to the reasonable satisfaction of the Landlord.

4. Permit entry

To permit the Landlord at all reasonable times on giving reasonable notice (except in case of emergency) to enter the Premises to exercise the rights excepted and reserved in this Underlease

5. Comply with notices to repair

5.1 To commence and complete all works for which the Tenant is liable under this Underlease as quickly as possible after service of a written notice by the Landlord requiring such works

5.2 If the Tenant does not commence such works within two months of service of such notice (or sooner if required) or does not complete them within a reasonable time (having regard to the obligation of the Tenant to complete them as quickly as possible) the Landlord may (without prejudice to the right of re-entry contained in this Underlease) enter the Premises to carry out such works the cost of which (including all Landlord's Expenses in connection with them) is to be repaid by the Tenant and recoverable by the Landlord as a debt on demand

6. Defects

To give immediate written notice to the Landlord on becoming aware of any defects in the Premises which may give rise to a liability or duty on the Landlord under common law or statute

7. Yielding up

7.1 Immediately prior to the end of the Term:-

7.1.1 to remove every sign or notice which the Landlord requires to be removed and (unless and to the extent that the Landlord agrees otherwise) to remove all tenant's fixtures and fittings furniture and effects from the Premises making good to the reasonable satisfaction of the Landlord all damage caused to the Building by such removal

7.1.2 (unless and to the extent that the Landlord agrees otherwise) to reinstate and restore the Premises to the same state and condition as they were in prior to the carrying out of any works to the Premises by the Tenant

7.1.3 so far as applicable to hand over to the Landlord (or if requested to provide copies of) any:-

(a) files registers or management plans (including any relating to asbestos) required to be maintained under health and safety legislation in relation to the Premises

(b) EPC for the Premises together with details of the reference number of such EPC (if not apparent from the copy)

(c) air-conditioning inspection report relating to any air-conditioning system serving the Premises and obtained by the Tenant as the relevant person under the EPB Regulations

(d) records in relation to the Premises (including any underlet part of the Premises) made for the purposes of complying with the Regulatory Reform (Fire Safety) Order 2005 including any records of findings following a fire risk assessment of the Premises (or any underlet part)

7.2 At the end of the Term quietly to yield up the Premises to the Landlord in such repair and condition as complies with the Tenant's obligations under this Underlease

8. Refuse and deleterious substances

8.9 Not to burn any rubbish on the Premises or the Common Parts and not to deposit any rubbish on the Premises or the Common Parts other than in proper containers (as to those in the Common Parts being as provided by the Landlord) and to ensure that rubbish or refuse containers on the Premises are regularly emptied

8.10 Not to permit any substance which is or might become of a dangerous hazardous polluting or contaminative nature or which might in any way materially adversely affect or damage the Building any Service Media other land or water or the environment or cause significant harm to human health to be in on or under or to escape from the Premises and if the Tenant becomes aware of any such substance in on under or escaping from the Premises to give immediate written notice of it to the Landlord and to remove or remediate it in compliance with the requirements of the Landlord or any competent authority PROVIDED THAT:

8.10.1 the Tenant may keep or use such materials as are necessary for its laboratory operations in accordance with appropriate laboratory health and safety procedures all applicable statutory requirements and in accordance with the regulations of the Campus (as defined in the Superior Lease);

8.10.2 the use of the Premises as laboratories for research and development activities in accordance with relevant regulations and any requisite regulations consents or licence and in accordance with the requirements of the insurers of the Building notified in writing to the Tenant shall not in itself constitute a breach of this covenant.

9. Overloading and damage

Not to overload the Premises nor damage overload or obstruct any Service Media or the Retained Premises

10. Fire precautions

10.1 To comply with all requirements from time to time of any competent authority in relation to fire precautions and means of escape affecting the Premises and to keep sufficient firefighting and extinguishing apparatus and fire alarm and smoke detection apparatus in and about the Premises open to inspection and properly maintained and not to obstruct the access to or means of working them nor any means of escape from the Premises

10.2 Whenever requested by the Landlord to provide copies of or make available for inspection any records in relation to the Premises (including any underlet part of the Premises) made for the purposes of complying with the Regulatory Reform (Fire Safety) Order 2005 including any records of findings following a fire risk assessment of the Premises (or any underlet part)

11. Prohibited use and nuisance

11.1 Not to use the Premises for any noisy offensive dangerous illegal or immoral purpose nor for residential or sleeping purposes nor for gambling or betting PROVIDED THAT the use of the Premises as laboratories for research and development activities shall not in itself be a breach of this covenant

11.2 Not to hold on the Premises any political meeting or public show or spectacle or any sale by auction

11.3 Not to do anything on the Premises or on any part of the Common Parts or any land or building over which any right granted by this Underlease is exercised which may cause a legal nuisance damage or disturbance or obstruction to the Landlord or any occupier of any other part of the Building or any owner or occupier of other land PROVIDED THAT the use of the Premises for as laboratories for research and development activities shall not in itself be a breach of this covenant

11.4 Not to use the Premises as a government or government agency claims office where members of the public may call without appointment

11.5 Not to permit the Premises to be occupied or used by any person entitled to sovereign diplomatic or similar immunity

12. Permitted Use

Not to use the Premises otherwise than for the Permitted Use

13. Alterations

13.1 Not (except as may be authorised under paragraphs 13.2 and 14 of this schedule) to make any alteration or addition to the Premises nor to erect any telecommunications mast at the Premises

13.2 Not without the prior written consent of the Landlord (such consent not to be unreasonably withheld and to be given by deed unless the requirement for a deed is expressly waived by the Landlord in writing):-

13.2.1 to make any internal non-structural alteration or addition to the Premises except that no such consent will be required for the Tenant to install alter or remove non-structural demountable non-combustible office partitioning which does not adversely affect any firefighting lighting heating cooling ventilating or air conditioning equipment or system serving the Retained Premises

13.2.2 to erect on the exterior of the Premises any pole mast aerial dish security equipment or similar apparatus

13.2.3 to make any alteration or addition to the Premises which in the Landlord's reasonable opinion materially adversely affects the energy efficiency or Asset Rating or (where applicable) the Operational Rating of the Premises or the Building

PROVIDED ALWAYS THAT before giving consent under this paragraph the Landlord may require the submission by the Tenant to the Landlord of sufficient information to enable the Landlord to assess the impact of the proposed alteration on the energy efficiency or Asset Rating or (where applicable) the Operational Rating of the Premises or the Building

13.3 Not to impede access to any Service Media

13.4 To supply to the Landlord all plans and specifications necessary to identify any proposed works whether or not requiring the consent of the Landlord and to carry out such works only in accordance with such plans and specifications in a good and workmanlike manner and (if the Landlord's consent is required but not otherwise) to the reasonable satisfaction of the Landlord

13.5 After commencing any alterations (whether or not they require the consent of the Landlord) to complete them within such period as the Landlord may reasonably require and in any event before the end of the Term

13.6 To pay to the Landlord on demand the cost of any works to the Heating Systems that may be required as a result of any alterations carried out by the Tenant

13.7 On completion of any alterations and if required by the EPB Regulations to obtain a valid EPC for the Premises and deliver a copy to the Landlord within 7 days of its receipt together with details of the reference number of such EPC (if not apparent from the copy)

13.8 If the Tenant fails to observe the covenants contained in this paragraph the Landlord may enter the Premises and reinstate or remove any unauthorised alterations additions equipment or systems and make good all damage caused by such reinstatement or removal and the cost of such work (including Landlord's Expenses) is to be repaid by the Tenant and recoverable by the Landlord as a debt on demand

14. Signs and advertisements

Not to exhibit any form of flag sign advertising or notification material which is visible from the exterior of the Premises without the prior written consent of the Landlord (such consent not to be unreasonably withheld)

15. Easements

15.1 Not to obstruct any window or light or abandon any easement from time to time enjoyed by the Premises

15.2 Upon becoming aware to give immediate written notice to the Landlord of any encroachment on or circumstance which might result in the acquisition of any easement or other right over the Premises and at the Landlord's entire cost to take or join in such proceedings or take such other steps as the Landlord may reasonably require to prevent any such acquisition

16. Alienation

16.1 Not to:-

16.1.1 part with or share possession or occupation of the whole or any part of the Premises except as may be permitted in accordance with the provisions of this paragraph 16

16.1.2 hold the whole or any part of the Premises on trust for another

16.1.3 assign sub-underlet or charge any part of the Premises as distinct from the whole

16.1.4 charge the whole of the Premises without the prior written consent given by deed of the Landlord (such consent not to be unreasonably withheld or delayed) save in respect of a floating charge to a bona fide financial institution in which case no consent is required

16.1.5 assign the whole of the Premises without the prior written consent given by deed of the Landlord (such consent not to be unreasonably withheld or delayed) PROVIDED THAT the Landlord will be entitled (for the purposes of section 19(1A) of the Landlord and Tenant Act 1927):-

(a) in addition to any other reasonable ground to withhold its consent in any of the circumstances set out in paragraph 16.3

(b) in addition to any other reasonable condition to impose all or any of the matters set out in paragraph 16.4 as a condition of its consent

16.2 The Landlord may abandon any of the circumstances set out in paragraph 16.3 and/or any of the conditions set out in paragraph 16.4 by giving written notice to that effect to the Tenant and from such time any circumstance or condition specified in the notice will be deemed to be deleted and of no further effect

16.3 The circumstances referred to in paragraph 16.1.5(a) are as follows:-

16.3.1 Where the proposed assignee is a Group Company or where the proposed assignee is an associated company of the Tenant (within the meaning of section 449 of the Corporation Tax Act 2010) and the Landlord reasonably considers that the proposed assignee is of materially lesser financial standing (as reported in their respective last three years profit and loss accounts and balance sheets) than the Tenant (aggregated with any surety or sureties for the Tenant) measured at:-

(a) either the date of this Underlease or at the date of the last permitted assignment (whichever is applicable) or

(b) (if the financial standing of the Tenant aggregated with any surety as referred to above is then greater) the date of the application to the Landlord for consent to the proposed assignment

and the proposed assignee does not provide additional financial security reasonably satisfactory to the Landlord to account for the said material difference in financial standing

16.3.2 Where the proposed assignee is the Surety

16.3.3 where the proposed assignee's surety is a surety under this Lease

16.3.4 where the proposed assignee's surety or guarantor is a party who remains liable under the tenant covenants under this Lease immediately prior to the assignment (but not a party giving the guarantees under paragraphs 16.3.1 and/or 16.3.2 of this schedule)

16.4 The conditions referred to in paragraph 16.1.5(b) are as follows:-

16.4.1 That where reasonable the Tenant enters into an authorised guarantee agreement (as defined in section 16 of the 1995 Act) containing (inter alia) provisions in substantially the same terms as those set out in schedule 7 subject to such amendments as the Landlord may reasonably require or as may be required to keep the agreement within the definition

16.4.2 That the surety (if any) (surety here meaning only the surety for the assigning tenant) is made a party to any authorised guarantee agreement entered into by the Tenant under paragraph 16.4.1 to guarantee the performance of the obligations of the Tenant under such authorised guarantee agreement on such terms as the Landlord may reasonably require

16.4.3 That all Rents due prior to the date of the assignment are paid to the Landlord by such date

16.4.4 That the proposed assignee provides a surety or sureties reasonably acceptable to the Landlord (if so reasonably required by the Landlord) to covenant with the Landlord in the terms contained in schedule 7 (mutatis mutandis)

16.5 Not to sub-underlet the whole of the Premises without the prior consent given by deed of the Landlord (such consent not to be unreasonably withheld or delayed) nor without procuring that:-

16.5.1 prior to the grant of any sub-underlease the sub-undertenant will execute a deed containing direct covenants with the Landlord

(a) to perform and observe the obligations of the sub-undertenant in the sub-underlease and the obligations of the Tenant under this Underlease (other than the obligation to pay the Rents) and

(b) (if the liability of the Tenant is disclaimed by or on behalf of the Tenant and if so required by the Landlord by written notice to the sub-undertenant within four months after such disclaimer) to take from the Landlord and execute and deliver to the Landlord a counterpart of a new underlease of the Premises or the premises sub-underlet as the case may be for the residue of the term of the sub-underlease unexpired at the date of such disclaimer at the same rents as are reserved from time to time by and subject to substantially the same covenants and provisions as are contained in the relevant sub-underlease and the sub-undertenant will on demand pay the Landlord's Expenses in connection with such new underlease

16.5.2 any sub-undertenant will (if the Landlord reasonably requires) provide a surety or sureties reasonably acceptable to the Landlord to guarantee the due performance by the sub-undertenant of its obligations in the sub-underlease in substantially the terms contained in schedule 7

16.5.3 each sub-underlease will be at a rent which will:-

(a) be not less than the open market rental value (without taking or giving a fine or premium or other valuable consideration) reasonably obtainable for the Premises at the time such sub-underlease is granted

(b) not be commuted or be payable more than one quarter in advance

16.5.4 each sub-underlease will contain covenants by the sub-undertenant:-

(a) not to assign further sub-underlet or charge any part of the premises sub-underlet as distinct from the whole

(b) not to part with possession or share the occupation of the whole or any part of the premises sub-underlet save by way of an assignment of the whole of them

(c) not to assign or charge the whole of the premises sub-underlet without obtaining the prior consent given by deed of the Landlord (such consent not to be unreasonably withheld or delayed)

(d) not to assign the whole of the premises sub-underlet without the assignee executing a deed containing direct covenants with the Landlord in the same terms as those set out in paragraph 16.5.1

16.5.5 each sub-underlease will otherwise be on terms corresponding with this Underlease (except the obligation to pay the Rents)

16.5.6 each sub-underlease contains an agreement validly excluding in relation to itself the provisions of sections 24 to 28 (inclusive) of the 1954 Act in accordance with section 38A of the 1954 Act

16.6 Not without the prior written consent of the Landlord (such consent not to be unreasonably withheld) to vary or waive the terms or to accept any surrender of any sub-underlease and to take all steps necessary to enforce such terms

16.7 Nothing contained in this paragraph will prevent the Tenant from sharing occupation of the Premises with any Group Company if the following conditions are fulfilled:-

16.7.1 Prior written notice is given to the Landlord of the intended occupation by the Group Company

16.7.2 No tenancy is created between the Tenant and the Group Company

16.7.3 The right of the Group Company to share occupation of the Premises will determine upon either the Tenant or the Group Company ceasing to be members of the same group (within the definition of Group Company contained in clause 1.1)

17. Register Underlease and devolutions

17.1 Within one month of the creation or disposition of any interest in or charge over the Premises to give written notice of it to the Landlord and produce a certified copy of any relevant document and to pay a reasonable registration fee not exceeding £50.00 plus VAT if demanded

18. Information about the Premises

18.1 From time to time on demand to provide the Landlord with full particulars of all interests in the Premises

18.2 To disclose such information as the Landlord may from time to time require in relation to any application or request made or particulars produced to the Landlord

18.3 If so requested by the Landlord to provide the Landlord with a copy of any air-conditioning inspection report relating to any air-conditioning system serving the Premises and obtained by the Tenant as the relevant person under the EPB Regulations

19. Landlord's costs

To pay to the Landlord on an indemnity basis all costs claims demands and expenses (including all Landlord's Expenses) properly incurred by the Landlord in contemplation of or in relation to or as a result of:-

19.1 any notice under sections 146 or 147 of the Law of Property Act 1925 and/or any proceedings pursuant to such notice (even if forfeiture is avoided otherwise than by relief granted by the court)

19.2 the preparation and service of any schedule of dilapidations during or within four months after the end of the Term

19.3 any breach of any obligation of the Tenant under this Underlease

19.4 any application for consent under this Underlease (except where consent is determined to have been unlawfully withheld) provided that any such costs must be reasonable

19.5 the provision of any information or assistance requested by the Tenant in connection with the supply or preparation of an EPC or DEC for the Premises provided that any such costs must be reasonable

20. Statutory requirements

20.1 At its own expense to comply with statute common law and all relevant codes of practice in relation to the Premises (whether or not such requirements are imposed upon the owner occupier or any other person)

20.2 To pay to the Landlord a due and fair proportion (to be determined by the Landlord acting reasonably) of all Landlord's Expenses in relation to compliance with such requirements or notices where they relate both to the Premises and to other land

21. Planning

21.1 To comply in all respects with the Planning Acts

21.2 Not to make any application under the Planning Acts without the prior written consent of the Landlord (such consent not to be unreasonably withheld)

21.3 To supply the Landlord with a copy of such application and copies of any plans and drawings submitted in connection with it and to keep the Landlord fully informed of the progress of any such application and its result

21.4 Not to initiate any development permitted as a result of any application under the Planning Acts without the prior written consent of the Landlord (such consent not to be unreasonably withheld)

21.5 Not to enter into any agreement or obligation or serve any purchase notice under the Planning Acts without the prior written consent of the Landlord

22. Energy Performance Certificates

22.1 To allow the Landlord and/or any person authorised by it to have access to all documentation data and information in the Tenant's possession or under its control reasonably required in order to:-

22.1.1 prepare an EPC for the Building

22.1.2 prepare a DEC for the Building (where appropriate)

22.1.3 comply with any duty imposed upon the Landlord under the EPB Regulations

and to co-operate with the Landlord and any persons so authorised so far as is reasonably necessary to enable them to carry out such functions

22.2 Where the Tenant wishes or is required by the EPB Regulations to obtain an EPC for the Premises (save where the provisions of paragraph 13.7 of this schedule apply):-

22.2.1 to notify the Landlord in writing before obtaining an EPC and if in response to such notice the Landlord confirms that it holds a valid EPC for the Premises or the Building to use such EPC for so long as it remains valid under the EPB Regulations and to reimburse the Landlord the reasonable cost of providing a copy of such EPC to the Tenant

22.2.2 if the Tenant obtains an EPC that invalidates or materially adversely affects any valid EPC for the Premises or the Building held by the Landlord of which the Tenant has notice to indemnify the Landlord in respect of any loss suffered as a consequence of the Tenant's action including (at the Landlord's discretion) the cost of obtaining a replacement EPC

22.2.3 to provide the Landlord with a copy of any EPC or DEC within 7 days of its receipt together with details of the reference number of such EPC or DEC (if not apparent from the copy)

23. Wireless Data Services

Not to operate Wireless Data Services so as to interfere with the lawful provision of Wireless Data Services in any other Lettable Premises or in any part of the Retained Premises or any adjoining or neighbouring premises

24. Notices

Within seven days of receipt (or sooner if required) to produce to the Landlord full particulars of any notice order permission or proposal in relation to the Premises and at the entire cost and reasonable request of the Landlord to make or join with the Landlord in making such objections or representations in respect of it as the Landlord reasonably requires save where to do so would materially adversely affect the Tenant's commercial interests at the Premises

25. Indemnity

To indemnify the Landlord against all actions proceedings claims demands direct losses costs expenses damages and liability (including any liability for any injury to any person or damage to any land or other property) and any court or tribunal orders or awards arising from any breach of any obligation of the Tenant under this Underlease or the state and condition of the Premises for which the Tenant is responsible or any use of the Premises or any act or omission of the Tenant provided that this indemnity shall not obviate the Landlord's common law duty to mitigate its loss

26. Notice boards

To permit the Landlord to fix and retain on the Premises a notice board (during the last six months of the Term) for the re-letting of the Premises and (at any time) for the sale of the Landlord's interest and to permit all persons authorised by the Landlord to view the Premises at reasonable hours upon reasonable notice provided that any such notice does not interfere with access of light to the Premises

27. Incumbrances

To comply with all covenants and other matters relating to the Premises or to any of the rights granted by this Underlease so far as contained or referred to in any documents specified in schedule 6 and so far as they are enforceable

28. The Common Parts and regulations

28.1 Not to park any vehicle on or so as to obstruct any roadways within the curtilage of the Building

28.2 Not to park any vehicle on any car parking spaces or areas within the curtilage of the Building other than the car parking areas within the Common Parts

28.3 Not to use the car parking areas within the Common Parts for the storage (whether temporary or permanent) of any materials or goods or the servicing repair or cleaning of any vehicle nor to permit petrol oil or other deleterious materials to be emptied on such spaces

28.4 Not to use any toilets within the Common Parts other than the Toilets

28.5 Not to obstruct the Common Parts

28.6 To comply with such reasonable regulations as the Landlord may from time to time make and notify to the Tenant in writing for the proper management of the Building and in case of any conflict between such regulations and this Underlease the terms of this Underlease will prevail

29. Value Added Tax

29.1 To pay all Value Added Tax in respect of all taxable supplies made to the Tenant under this Underlease or as the case may be to repay to the Landlord any Value Added Tax borne by the Landlord in respect of taxable supplies made to the Landlord (except to the extent in the latter case to which the Landlord recovers it) and in every case where under this Underlease the Tenant is obliged to pay an amount of money such amount shall be regarded as being exclusive of all Value Added Tax from time to time payable on it and the Landlord shall supply a valid VAT invoice to the Tenant in accordance with its statutory obligations

29.2 Not to take any action or permit any action to be taken which would result in the disapplication of the Landlord's option to tax (if applicable)

30. Superior Lease

30.1 Not to do omit suffer or permit in relation to the Premises any act or thing which would or might cause the Landlord to be in breach of the Superior Lease or which if done omitted suffered or permitted by the Landlord would or might constitute a breach of the obligations of the lessee contained in the Superior Lease or in any lease or leases superior to the Superior Lease

30.2 Without prejudice to the generality of the foregoing to operate its business at the Premises in accordance with the Ethos

Schedule 3

Landlord's covenants

1. Quiet enjoyment

That the Tenant paying the Rents and complying with its other obligations under this Underlease may peaceably hold and enjoy the Premises during the Term without any interruption by the Landlord or any person lawfully claiming through under or in trust for it

2. Superior Lease

To pay the rents reserved by the Superior Lease and perform the covenants on the part of the tenant contained in the Superior Lease

At the request of the Tenant (and subject to the Tenant providing a suitable indemnity for costs) to use all reasonable endeavours to enforce any obligations of the Superior Lessor to the Landlord

3. Superior Lease

If the Superior Lease is surrendered, the Landlord shall from the date of the surrender perform or procure the performance of obligations equivalent to the Superior Landlord's covenants immediately prior to the surrender of the Superior Lease

4. Superior Landlord's consent

At the expense of the Tenant to take reasonable steps to obtain the consent of the Superior Landlord whenever the Tenant makes an application for any consent required under this Underlease where the consent of the Superior Landlord to such an application is also required under the Superior Lease

5 Exercising rights of entry

Prior to exercising any of the rights of entry to the Premises reserved by paragraphs 1 and 2 of part 3 of Schedule 1 the Landlord shall (save in case of emergency) first agree with the Tenant (both parties acting reasonably) the time and duration of such entry into the Premises having regard to the sensitive experiments that will be carried on from time to time in the Premises and the Tenant shall use all reasonable endeavours to permit the Landlord to enter the Premises within 48 hours of the Landlord's request save where the Tenant's experiments will bona fide prevent the Landlord from accessing the Premises within such time period in which case the Tenant shall permit the Landlord to enter as soon as reasonably possible thereafter.

Schedule 4

Provisos

1. Re-entry

Without prejudice to any other right remedy or power of the Landlord it will be lawful for the Landlord or any person authorised by the Landlord to re-enter the Premises (or any part of them in the name of the whole) if:-

1.1 any Rents remain unpaid for twenty one days (whether formally demanded or not) or

1.2 there is any breach of any obligation of the Tenant under this Underlease or

1.3 the Tenant and/or the Surety (if any) becomes insolvent meaning:-

1.3.1 in relation to a body corporate:-

(a) a winding-up resolution is passed by a meeting of its members (otherwise than in connection with a member's voluntary winding up for the purposes of an amalgamation or a reconstruction that has the prior written approval of the Landlord) or

(b) a resolution is passed by a meeting of its directors to seek a winding up order or an administration order or to appoint an administrator or

(c) a winding up or administration order is made or

(d) it issues or its directors or the holder of a qualifying floating charge (as defined in Schedule B1 of the Insolvency Act 1986) issues a notice of appointment or of intention to appoint an administrator or

(e) it becomes subject to any voluntary arrangement or its directors take steps to obtain a moratorium (whether under Part I of the Insolvency Act 1986 or otherwise)

and sub-paragraphs (a) to (c) above shall also apply in relation to a partnership or limited partnership (as defined in the Partnership Act 1890 and the Limited Partnerships Act 1907 respectively) subject to the modifications referred to in the Insolvent Partnerships Order 1994 (SI 1994/2421) (as amended) and to a limited liability partnership (as defined in the Limited Liability Partnerships Act 2000) subject to the modifications referred to in the Limited Liability Partnerships Regulations 2001 (SI 2001/1090) or

1.3.2 in relation to an individual and where the relevant party is comprised of one or more individuals (whether or not in partnership together) in relation to any one of them:-

(a) a bankruptcy order is made against him

(b) a voluntary arrangement is made under Part VIII of the Insolvency Act 1986 or

1.3.3 in relation to any party:-

(a) a receiver (administrative or otherwise) is appointed over all or part of their assets or

(b) possession is taken of all or substantially all of their assets by a secured party or they become subject to an execution attachment sequestration or other legal order over all or substantially all of their assets or

(c) they make any general assignment composition or arrangement with or for the benefit of all or some of their creditors or

(d) they are unable to make payments to all or some of their creditors or

1.3.4 any analogous or equivalent proceedings actions or events to those referred to in paragraphs 1.3.1 to 1.3.3 above are instituted or occur in any jurisdiction other than England and Wales

AND upon re-entry the Term will terminate but without prejudice to any claim by the Landlord in respect of any antecedent breach of any obligation of the Tenant under this Underlease

2. Exclusions

2.1 Except where expressly granted by this Underlease the Tenant will not have:-

2.1.1 the benefit of any easement right or privilege

2.1.2 the benefit of or the right to enforce or to prevent the release or the modification of any covenant agreement or condition benefiting the whole or any part of the Building to which any land not comprised in the Building may from time to time be subject or

2.1.3 the benefit of or the right to enforce or to prevent the release or the modification of any covenant agreement or condition entered into by any tenant of any other Lettable Premises

2.2 The Landlord gives no express or implied warranty that the Premises are suitable for the Tenant's purposes or that the Permitted Use will be or remain a lawful or authorised use under the Planning Acts or otherwise

2.3 So far as the law allows the right of the Tenant (or any sub-undertenant) to compensation on quitting the Premises is excluded

2.4 Each of the provisions of this Underlease is severable and if any such provision is or becomes illegal invalid or unenforceable in any respect under the law of any jurisdiction that fact will not affect or impair the legality validity or enforceability in that jurisdiction of the other provisions of this Underlease or of that or any provision of this Underlease in any other jurisdiction

2.5 Nothing in this Underlease will be read or construed as excluding any liability or remedy in respect of fraud

3. Acceptance of rents

If the Landlord has reasonable grounds for believing that the Tenant is in breach of any of its obligations under this Underlease and refrains from demanding or accepting Rents then interest will be payable by the Tenant at two per cent per annum above the Interest Rate on such Rents for the period during which the Landlord so refrains such interest to be calculated on a daily basis

4. Notices

Any notice under or in relation to this Underlease will be deemed (whether or not that is actually the case) to be a notice required to be served for the purposes of section 196(5) of the Law of Property Act 1925 and the provisions of section 196 of that Act will extend to any such notice accordingly

5. Indemnity provisions

Where in this Underlease the Tenant and/or any Surety agrees to indemnify the Landlord the indemnity will be subject to the following terms:-

5.1 the Landlord will promptly give written notice to the Tenant and/or the Surety (as appropriate) of any claim demand or proceedings of which the Landlord is aware and which the Landlord reasonably considers may be covered by an indemnity contained in this Underlease (for the purposes of this paragraph 5 a **"Claim"**)

5.2 the Landlord will promptly give the Tenant and/or the Surety all details of any Claim as are in its possession or actual knowledge or which could reasonably be obtained by the Landlord

5.3 the Landlord will keep the Tenant and/or the Surety informed as to the progress of any Claim and will have proper regard to the Tenant's and/or the Surety's written representations to the Landlord regarding the Claim

5.4 to the extent to which the Landlord is able to do so (having regard to the ability of the Landlord to settle or compromise a Claim without the involvement of the Insurers of the Building) the Landlord will not settle or compromise any Claim without the consent of the Tenant and/or the Surety (such consent not to be unreasonably withheld by either the Tenant or the Surety) except under an order of the Court (other than a consent order)

6. Landlord's right to redevelop

The Landlord will be free to build on and use any other part of the Building and any nearby or adjoining land or buildings of the Landlord in any way notwithstanding that such building or use results in any reduction in the flow of light air access to and/or amenities enjoyed by the Premises PROVIDED THAT reasonably acceptable and convenient alternative means of access and/or amenities are provided and that the Tenant's use and enjoyment of the Premises for the Permitted Use is not materially adversely affected thereby

7. Tenant's property

7.1 If any property of the Tenant remains at the Premises after the Tenant has vacated the Premises following the end of the Term and the Tenant fails to remove it within 7 days after a written request from the Landlord or if having made reasonable efforts the Landlord is unable to locate the Tenant within 14 days from the first attempt to make such request then the Landlord may sell such property as the agent of the Tenant

7.2 The Landlord will account to the Tenant for the proceeds of sale of such property within 14 days of the date of sale less the costs incurred in connection with such sale PROVIDED THAT if having made reasonable efforts the Landlord is unable to locate the Tenant then the Landlord may retain the proceeds of sale absolutely unless the Tenant claims them (less the costs of sale) within 6 months of the end of the Term

7.3 The Tenant will indemnify the Landlord against any liability incurred to any third party whose property is sold by him in the mistaken belief held in good faith that the property belonged to the Tenant

8. Third party rights

8.1 Nothing in this Underlease is intended to confer on any person any right to enforce any term of this Underlease which that person would not have had but for the Contracts (Rights of Third Parties) Act 1999 save as provided in paragraphs 8.2 and 8.3 below

8.2 The Landlord and the Tenant agree that the Superior Lessor may in its own right enforce paragraph 30.2 of schedule 2 to this Underlease subject to and in accordance with the provisions of paragraph 8.3 below and the provisions of the Contracts (Rights of Third Parties) Act 1999

8.3 No right of the Landlord and the Tenant to agree any amendment variation waiver or settlement under or arising from or in respect of this Underlease will be subject to the consent of any person who has rights under this Underlease solely by virtue of the Contracts (Rights of Third Parties) Act 1999

9. Common Parts

The Landlord acting reasonably may from time to time change the location area or arrangements for use by the Tenant of any part of the Common Parts or Service Media so long as there remains available for the benefit of the Premises rights reasonably commensurate with those granted by this Underlease and that the Tenant's use and enjoyment of the Premises for the Permitted Use is not materially adversely affected thereby

10. Data Protection Act consent

For the purposes of the Data Protection Act 1998 or otherwise the Tenant and any Surety agree that information held by the Landlord relating to this Underlease may be disclosed to third parties in connection with the management of and/or any disposal or other dealing with the whole or any part or parts of the Landlord's interest in the Building

11. Environmental Liability

11.1 In this paragraph 11:

"Contaminated Land Regime" means the contaminated land regime under Part 2A of the Environmental Protection Act 1990 (as amended from time to time) and any statutory instrument or guidance issued under it (from time to time)

"Enforcing Authority" means the relevant regulator for the Premises under the Contaminated Land Regime

"Environment" means the natural and man-made environment including all or any of the following media, namely air, water and land (including air within buildings and other natural or man-made structures above or below the ground) and any living organisms (including man) or systems supported by those media

"Environmental Law" means all applicable laws, statutes, secondary legislation, bye-laws, common law, directives, treaties, judgments and decisions of any court or tribunal, codes of practice compliance with which is a legal requirement (as amended from time to time) in so far as they relate to the protection of the Environment

"Hazardous Substances" means any substance in solid, liquid or gaseous form which, alone or in combination with others, is capable of causing harm to the Environment

11.2 Notwithstanding any other provisions in this Lease, the Landlord and Tenant agree that:

11.2.1 between the Landlord and the Tenant, the Landlord shall assume any liability under Environmental Law (including, without limitation, any liability under the Contaminated Land Regime) arising in respect of Hazardous Substances in, on, under or migrating from the Premises or the Building before the date of this Lease but the Tenant will have the burden of proof to show that any such Hazardous Substances existed prior to the date of this Lease and were not caused or knowingly permitted by the Tenant (and for the avoidance of doubt where the Tenant fails to establish this the Tenant shall assume such liability);

11.2.2 the provisions of this paragraph constitute an agreement on liabilities under the Contaminated Land Statutory Guidance published by the Department for Environment, Food and Rural Affairs in April 2012;

11.2.3 if the Enforcing Authority serves a notice under the Contaminated Land Regime on either party, either party may produce a copy of this paragraph to that Enforcing Authority for the purposes of paragraph 7.29 of the Contaminated Land Statutory Guidance (or any equivalent provisions under statutory guidance which replaces or amends it), regardless of any confidentiality agreement that may exist between the parties relating to this Lease or any of its provisions;

11.2.4 Neither party shall challenge the application of the agreement on liabilities set out in this paragraph

Schedule 5

Insurance

1. Covenant to insure and reinstate

1.1 Without prejudice to the generality of paragraph 2 of schedule 3 the Landlord covenants with the Tenant to take all reasonable steps to comply with its obligations under the Superior Lease to insure the Building at all times and to reinstate and rebuild in accordance with the provisions of the Superior Lease in the event that the Premises or any Common Parts reasonably required for the use of the Premises or any parts thereof are damaged or destroyed by any Insured Risk save to the extent that the insurance is vitiated by some act or default of the Tenant and SUBJECT TO the payment by the Tenant to the Landlord of any money payable under paragraph 4 of this schedule which the Landlord will (following such payment) lay out in such reinstatement or rebuilding

1.2 The Landlord will produce to the Tenant on request (but not more often than once in any period of twelve months) reasonable evidence from the Insurers of the terms and subsistence of any policy or policies of such insurance and details of any material changes

1.3 The Tenant will give the Landlord written notice of the estimated reinstatement cost of any fixtures and fittings installed from time to time by the Tenant which may become landlord's fixtures and fittings

1.4 The Landlord will use all reasonable endeavours to procure that the terms of the insurance of the Building allow the Tenant's interest to be noted on the policy or provide for automatic noting in the event of a claim and contain a waiver by the Insurers of rights of subrogation against the Tenant on such terms as are available from the Insurers

1.5 The Landlord will at all times insure against loss of the Yearly Rent for a period of three years

2. Insurance Rent

The Tenant will pay to the Landlord the Insurance Rent in accordance with clause 2.2.1

3. Reinstatement prevented and determination

3.1 If at the date that is three years from and including the date of damage or destruction all destruction or damage by any Insured Risk to the Building or any of the Common Parts reasonably required for the use of the Premises in accordance with this Underlease has not been made good and the Premises are still unfit for or incapable of occupation and use the Landlord or the Tenant may by written notice to the other given at any time within six months after such date and whilst the Premises are still unfit for use terminate the Term with immediate effect and the Landlord will be

entitled to all the insurance money PROVIDED THAT such termination will be without prejudice to any claim in respect of any antecedent breach of the obligations under this Underlease

3.2 any such notice given by the Tenant will only have effect if the Tenant has complied with its obligations under paragraph 4 of this schedule and any such notice given by the Landlord will only have effect if the Landlord has complied materially with its obligations at paragraph 1.1 of this schedule

4. Further payments by the Tenant

4.1 If the payment of any insurance money is refused owing to some act or default of the Tenant the Tenant will pay to the Landlord the amount so refused within fourteen days of demand

4.2 If any excess to which any policy of insurance relating to the Premises is subject becomes applicable, where the insurance claim in respect of which the excess is payable relates to the whole or any part of the Premises and/or the whole or any part of the Common Parts the Tenant will pay to the Landlord the amount of such excess or a fair proportion of the total excess which applies to the Building within fourteen days of written demand

5. Suspension of Rent

If any part of the Building or any of the Common Parts reasonably required for the use of the Premises in accordance with this Underlease are destroyed or damaged by any Insured Risk so as to render the Premises or a material part thereof unfit for or incapable of occupation and use or inaccessible the Rent or a fair proportion of it according to the nature and extent of the damage sustained will be suspended (save to the extent that the insurance money is irrecoverable owing to some act or default of the Tenant) until the Premises cease to be unfit for or incapable of occupation and use and/or inaccessible or three years from the date of damage or destruction (whichever is the earlier) PROVIDED THAT any dispute as to the extent proportion or period of such suspension will be determined by an arbitrator to be agreed upon by the Landlord and by the Tenant or at the request of either of them to be nominated by or on behalf of the President for the time being of the Royal Institution of Chartered Surveyors in accordance with the Arbitration Act 1996

6. Benefit of other insurances

The Tenant will apply all money which it receives by virtue of any insurance of the Premises in making good the loss or damage in respect of which it has been received

7. Insurance becoming void

The Tenant will:-

7.1 not cause any policy of insurance covering the Premises or any other land to become void or voidable or the rate of premium of any such policy to be increased

7.2 comply with all requirements from time to time of the Insurers in relation to the Premises which have been notified in writing to the Tenant

8. Notice by Tenant

The Tenant will give written notice to the Landlord as soon as practicable after it becomes aware of any event which might affect or give rise to a claim under any policy of insurance covering the Premises

9. Uninsured Risks

If the Premises are wholly or substantially damaged or destroyed by a risk that was an Insured Risk at the date of this Lease but, at the date of the damage to or destruction of the Premises, insurance is no longer available in respect of that risk through reputable and substantial insurers at normal commercial rates:

9.1 the provisions of paragraph 1 of this Schedule will apply as if the damage to or destruction of the Premises had been caused by an Insured Risk and will continue to apply until the Premises have been rebuilt and reinstated and are fit for occupation and use;

9.2 neither the Landlord nor the Tenant will be under any obligation to repair, decorate, rebuild or reinstate the Premises or to contribute towards the costs of doing so except in accordance with the terms of this paragraph 9

9.3 this Lease will end on the date one year after the date of the damage to or destruction of the Premises unless, during that year, the Landlord serves a notice on the Tenant in which the Landlord elects either to reinstate or rebuild the Premises or to end this Lease on an earlier date

9.4 if the Landlord elects to reinstate or rebuild the Premises, it will do so at its own cost and expense and the provisions of paragraphs 1 and 3 of this Schedule will apply as if the damage was caused by an Insured Risk and as if the reference to the date of expiry of the Landlord's loss of rent insurance were to the date that is three years after the date of the Landlord's election to reinstate the Premises; and

9.5 the provisions of paragraph 5 will apply as if the damage was due to an Insured Risk

Schedule 6

The matters and the documents (if any) containing incumbrances to which the Premises are subject

1 The Premises are let subject to all matters referred to in the agreement for the grant of this Underlease dated 15 June 2016 and made between the Landlord (1) the Tenant (2) and the Surety (3)

2. The incumbrances contained in the entries in the property and charges registers of title number CB303470 as at the date of this Lease and title number CB406367 as at the date of this Lease (except in either case charges to secure the repayment of money)

Schedule 7

Covenants by Surety

1. The Surety will procure the punctual payment of the Rents and the observance and performance of all the obligations of the Tenant under this Underlease and any authorised guarantee agreement given by the Tenant upon any assignment of this Underlease and in the case of any default the Surety will on demand pay such Rents and observe and perform such obligations as if the Surety instead of the Tenant were liable therefor as a principal obligor and not merely as a surety

2. The Surety agrees with the Landlord as a primary obligation to keep the Landlord indemnified on demand against all actions proceedings claims demands losses costs expenses damages and liability arising from any failure by the Tenant to pay the Rents and/or observe and perform such obligations or as a result of any obligation of the Tenant under this Underlease being or becoming unenforceable

3. The Surety agrees with the Landlord that this guarantee will take effect immediately on the grant (or the assignment as appropriate) of this Underlease to the Tenant and will remain in force until the Tenant is released by law (otherwise than by disclaimer) from liability under or in respect of this Underlease

4. If the liability of the Tenant is disclaimed by or on behalf of the Tenant the Surety will (if so required by the Landlord by written notice to the Surety within four months after such disclaimer) take from the Landlord and execute and deliver to the Landlord a counterpart of a new underlease of the Premises for the residue of the Contractual Term unexpired at the date of such disclaimer at the same Rents as are reserved from time to time by and subject to the same covenants and provisions as are contained in this Underlease (mutatis mutandis) and the Surety will on demand pay the Landlord's Expenses in connection with such underlease

5. Without prejudice to any other rights the Landlord may have against the Surety under this Underlease or at common law if the Landlord does not require the Surety to take a new underlease of the Premises pursuant to paragraph 4 of this schedule the Surety will nevertheless on demand pay to the Landlord a sum equal to the Rents that would have been payable but for the disclaimer during the period of twelve months from and including the date of the disclaimer (or until the end of the Term if that occurs sooner) less any Rents received by the Landlord from reletting the Premises and the Surety will on demand pay the Landlord's Expenses and agents' fees in connection with such reletting

6. The insolvency of the Tenant will not affect the liability of the Surety under this Underlease and any money received or recovered by the Landlord from the Surety may be placed in a separate or suspense account by the Landlord without any obligation on the Landlord to apply it in or towards the discharge of the Tenant's obligations under this Underlease so as to preserve the Landlord's right to prove in any insolvency of the Tenant in respect of the whole of the Tenant's indebtedness to the Landlord under this Underlease

7. If any claim is made against the Surety by the Landlord in relation to the obligations of the Surety under this Underlease the Surety will not make any claim against the Tenant for an indemnity if the Tenant becomes the subject of any voluntary arrangement (whether under Part I of the Insolvency Act 1986 or otherwise)

8. The Surety will at the request of the Landlord execute any document supplemental to or entered into pursuant to this Underlease to acknowledge that the Surety is bound and that the rights of the Landlord are not affected and the obligations of the Surety are not released by such document

9. The obligations of the Surety under this Underlease are in addition to any other right or remedy of the Landlord and will not be discharged diminished or in any way affected by:-

9.1. any time or indulgence granted by the Landlord to the Tenant or any neglect or forbearance of the Landlord in obtaining payment of the Rents or enforcing the obligations of the Tenant under this Underlease or

9.2. any refusal by the Landlord to accept Rents tendered at a time when the Landlord was entitled (or would after service of the appropriate statutory notice have been entitled) to re-enter the Premises or

9.3. any surrender by the Tenant of part of the Premises in which event the liability of the Surety will continue in respect of the part of the Premises not so surrendered after making any necessary apportionments under section 140 of the Law of Property Act 1925 or

9.4. any variation of this Underlease or other act omission matter or thing (other than a release by deed given by the Landlord and subject always to the provisions of section 18 of the 1995 Act) by which but for this provision the obligations of the Surety under this Underlease would have been so discharged diminished or affected

10. The Surety will join as a party to any authorised guarantee agreement given by the Tenant pursuant to the alienation provisions of this Lease to guarantee the performance of the Tenant's obligations under such authorised guarantee agreement on such terms as the Landlord may reasonably require

11. Any provision of this schedule rendered void or unenforceable by the 1995 Act is to be severed from all remaining provisions which are to be preserved

Schedule 8

Services and the Service Charge

Part 1

The Service Charge

1. Definitions

In this schedule the following expressions have the following meanings unless the context otherwise requires:-

"Annual Expenditure": the aggregate expenditure properly incurred or to be incurred by the Landlord during a Service Year in or incidental to the provision of or in respect of all or any of the Services after giving credit for:-

(a) any insurance money received by the Landlord under any policy in relation to the Building which the Landlord is obliged to effect under this Underlease and

(b) any amount received by the Landlord pursuant to any agreement covenant duty liability warranty or representation on the part of any building contractor architect or employer's agent surveyor engineer or other consultant workman or contractor responsible for the design construction or supervision (or the guarantor for any such persons) of any works on the Building carried out as part of the Services the cost of which has been included in the Annual Expenditure

PROVIDED THAT such expenditure will not include:-

(i) any initial costs incurred in relation to the original design and construction of the Building

(ii) any setting up costs that are reasonably to be considered part of the original development cost of the Building (including the provision of a backup generator)

(iii) any costs incurred in improving (as opposed to necessary repairs or replacements) or redeveloping the Building or any part of it

(iv) such costs as are matters between the Landlord and any tenant or occupier of Lettable Premises including the cost of enforcing covenants for the payment of rent any costs incurred in letting other Lettable Premises and costs associated with the conduct of rent reviews and applications for landlord's consent and costs associated with the demand and collection of rent

(v) any costs relating to any repairs or other works required as a result of any Inherent Defect

(vi) any costs attributable to the maintenance of any Lettable Premises or any proportion of Annual Expenditure attributable to Lettable Premises that are unoccupied or occupied by the Landlord

(vii) any costs recovered by the Landlord pursuant to any warranty or guarantee from which it benefits in relation to the initial design and construction of the Building

"Provisional Service Charge": the amount which in the reasonable opinion of the Landlord's surveyor or its managing agents or accountants represents a fair estimate of the Service Charge for the Service Year in question

"Service Charge": the fair proportion properly attributable to the Premises of the Annual Expenditure as determined from time to time by the Landlord's surveyor whose decision will be final except in case of manifest error

"Services": the services facilities amenities and items of expenditure specified in part 2 and part 3 of this schedule

"Service Year": a calendar year expiring on 31 July or such other annual period as the Landlord may in its sole discretion decide

2. Landlord's obligation to provide the Services

2.1 Subject to payment by the Tenant of the Service Charge and to the provisions of this schedule 8 the Landlord:-

2.1.1 will provide the mandatory Services set out in part 2 of this schedule and

2.1.2 may provide the discretionary Services set out in part 3 of this schedule

2.2 PROVIDED THAT:-

2.2.1 the Landlord will not be liable to the Tenant in respect of any failure or interruption in any of the Services by reason of necessary repair maintenance or replacement of any installations or apparatus or their damage or destruction or by reason of mechanical or other defect or breakdown or frost or other inclement conditions or shortage of fuel materials or labour or any other cause beyond the reasonable control of the Landlord but the Landlord will procure that any such Services are restored as soon as possible

2.2.2 the Landlord may withhold add to extend vary or alter any of the Services set out in part 3 of this schedule from time to time PROVIDED THAT in so doing the Landlord complies with the principles of good estate management in respect of the Building and acts reasonably in all the circumstances and notifies the Tenant in advance in writing of any changes and the estimated cost implications

2.2.3 if at any time during the Term the property comprising the Building is increased or decreased on a permanent basis or the benefit of any of the

Services is extended on a like basis to any adjoining or neighbouring property or if some other event occurs a result of which is that the Service Charge is no longer appropriate to the Premises the Service Charge will be varied with effect from the beginning of the Service Year following such event in such a manner as may be determined to be fair and reasonable in the light of the event in question by the Landlord's surveyor whose decision will be final

3. Statement of Annual Expenditure

3.1 The Landlord will as soon as practicable and in any event within the period of three months after the end of each Service Year prepare and submit to the Tenant a statement of the Annual Expenditure for that Service Year containing a fair summary of the expenditure referred to in it (including any sums credited) and showing the Service Charge for that Service Year and upon such statement being certified by the Landlord's surveyor or its managing agents or accountants it will be conclusive evidence for the purposes of this Underlease of all matters of fact referred to in the statement (except in the case of manifest error)

3.2 The Landlord may (acting reasonably) include in any such statement such proper provision calculated in accordance with the principles of normal accounting practice and good estate management for expenditure in any subsequent year as the Landlord may from time to time reasonably consider appropriate

3.3 Any omission by the Landlord to include in any such statement any sum expended or liability incurred in that Service Year will not preclude the Landlord from including such sum or the amount of such liability in the account for the subsequent year

3.4 During the period of four months from the date of the issue of any such statement the Tenant will be entitled to raise reasonable enquiries in respect of the statement and the Landlord will deal with any such enquiries promptly and efficiently and will make relevant supporting documentation available for inspection and the Tenant will reimburse the Landlord on demand all reasonable costs incurred by the Landlord in providing copies of any such documentation that may be requested by the Tenant

4. Payment of the Service Charge

4.1 The Tenant will pay to the Landlord on account of the Service Charge:-

4.1.1 on each Quarter Day for the period from and including the Service Charge Commencement Date to the end of the current Service Year one quarter of the Initial Service Charge the first (duly apportioned) payment to be made on the date of this Underlease and

4.1.2 on each subsequent Quarter Day one quarter of the Provisional Service Charge

4.1.3 within 14 days of demand a sum equal to the costs actually incurred by the Landlord of providing additional Services to the Common Parts and/or the Premises at the request of the Tenant and where such additional Services are

used by the Tenant together with any other tenant or occupier of Lettable Premises the Tenant will pay a fair proportion of such costs as determined from time to time by the Landlord's surveyor whose decision will be final)

4.2 If the Service Charge for any Service Year:-

4.2.1 exceeds the Initial Service Charge or the Provisional Service Charge payments made on account of the Service Charge (as the case may be) the excess will be paid by the Tenant to the Landlord within 14 days of demand provided the relevant statement of Annual Expenditure has already been provided to the Tenant

4.2.2 is less than such payments on account the overpayment will be allowed by the Landlord to the Tenant as a credit against Service Charge to become due or (in the Service Year ending on or after the expiry of the Term) will be repaid by the Landlord to the Tenant on demand

5. Continuation

The provisions of this schedule will continue to apply notwithstanding the end of the Term but only for the purposes of calculation and payment of the Service Charge for the period down to the end of the Term

Part 2

The Mandatory Services

1. Maintaining repairing preserving protecting decorating and where beyond economic repair renewing or replacing the Retained Premises and the Common Media

2. Operating inspecting maintaining altering repairing cleaning and where beyond economic repair renewing and replacing the Heating Systems and all other plant and machinery serving the Building including lifts and lift plant (excluding for the avoidance of doubt the goods lift which is included within the Premises) window cleaning hoists and tracks and the costs of all maintenance contracts entered into by the Landlord in relation to them

3. Providing via the Heating Systems appropriate and adequate hot water heating cooling and ventilation to the Building to such temperatures and for such periods as the Landlord acting reasonably may from time to time consider adequate

4. Providing maintaining repairing and where beyond economic repair renewing any fire alarm system and smoke detection apparatus and all firefighting and detection equipment in or on the Building including all sprinklers hoses and dry risers and all works necessary to comply with all requirements of the appropriate authority in relation to fire precautions and any requirements of the Insurers

5. Keeping the Common Parts cleaned and maintained to a reasonable standard and adequately lit where appropriate

6. Providing hot and cold water to the Toilets and Showers (including the wash basins) in the Common Parts

7. Providing maintaining repairing and where beyond economic repair renewing electric hand driers and providing an adequate supply of soap paper towels and such other items as the Landlord considers appropriate in the toilets in the Common Parts

8. Cleaning (both inside and outside) all windows in the Building other than those which the Tenant or any other tenant in the Building is obliged to clean

9. To clean regularly the carpets and other floor coverings in the Common Parts

10. Complying with all Acts of Parliament relating in any way to the Building its occupation or use and with any notice from any competent authority

11. Any gas electricity oil or other fuel water and telephones used in providing any Services

12. Providing maintaining and repairing the secure entry system to gain access into and egress from the Building.

13. Equipping furnishing and carpeting from time to time the Common Parts.

14. Providing maintaining repairing and where beyond economic repair renewing any equipment including alarms gates barriers means of surveillance fencing and lighting and security services for the security of the Building

15. Providing any dustbins or other similar receptacles for refuse (non clinical waste) for the Building and refuse collection

16. Providing maintaining repairing and where beyond economic repair renewing directional signs and other notices in or upon the Building

17. Maintaining keeping tidy and planting any area of land within the curtilage of the Building

18. Provision of a 100% back-up power supply

Part 3

The Discretionary Services

1. Abating a nuisance in so far as such nuisance is not the liability of or attributable to the fault of the Tenant or any other tenant in the Building

2. Contributing towards the expense of making repairing rebuilding or cleansing any roads pavements sewers drains pipes party walls structures or fences or other conveniences which may belong to or be used for the Building in common with any adjoining or neighbouring premises

3. Taking any steps reasonably deemed by the Landlord to be desirable or expedient in the interests of good estate management for making representations against or otherwise contesting the incidence of the provisions of any Act of Parliament affecting or allegedly affecting the Building or any part of it and for which no tenant of the Landlord is directly responsible

4. Commissioning obtaining preparation and/or provision of any EPC and/or (where applicable) any DEC in relation to the Building including the fees costs expenses and disbursements of any assessor engaged to prepare the EPC

5. Complying with the obligations of the lessee contained in the Superior Lease (except regarding payment of the rents thereby reserved) and save to the extent that the Tenant is liable therefor under this underlease

6. Employing staff or independent contractors or labour for the provision of the Services

7. Providing materials and equipment needed from time to time for the proper performance of the duties of any staff

8. Providing such further services as may from time to time be consistent with the principles of good estate management and/or preserving the amenities of the Building

9. Employing or retaining any solicitor accountant surveyor valuer architect engineer managing agent or management company or other professional consultant or adviser in connection with the management administration repair and maintenance of the Building including the preparation of any accounts certificates and statements relating to Annual Expenditure

10. If the Landlord (or any company subsidiary to or associated with the Landlord) fulfils the duties normally carried out by a managing agent a management fee not in excess of the sum reasonably and properly payable to an independent managing agent but not so as to result in a duplication of work or charges payable hereunder

11. All rates taxes and outgoings of any kind charged in respect of the Retained Premises (but not any tax payable by the Landlord on receipt of rent or which arises from a dealing with the Landlord's interest in the Retained Premises)

12. Providing equipping and operating reception facilities for persons visiting the Building

13. Any other reasonable and proper expenses incurred by the Landlord in respect of the Retained Premises (except such as any tenant or other occupier is liable to pay (including the Landlord where in occupation))

14. Interest (at not more than the Interest Rate) on money disbursed by the Landlord in providing any of the Services prior to reimbursement

Schedule 9

Provisions Referred to in Clause 8

The Further Lease entered into pursuant to clause 8 will be on the same terms and conditions as this Lease except that:-

1. It will not contain provisions equivalent to clause 8 and this schedule 9

2. The definition of the **"Rent"** in clause 1.1 will be re-designated as the **"Initial Rent"** and will be the Rent payable under this Lease as at the expiry of the Term (or if payment has been suspended or restricted the Rent which would have been payable had there been no suspension or restriction)

3. The definition of the **"Rent Commencement Date"** in clause 1.1 will be the 12th day of December 2021

4. The definition of the **"Term"** in clause 1.1 will be the term of years to be granted by the Further Lease as provided in clause 8

5. The following new definitions will be inserted into clause 1.1:-

   "Previous Lease": The previous lease of the Premises dated 2 March 2017 between Imperial College of Science Technology and Medicine (1) Convergence Pharmaceuticals Limited (2) and Biogen Idec Limited (3)

   "Review Date": The 12th day of December 2021

   "Specification": the lab suite specification annexed at appendix 1

   "Yearly Rent" the Initial Rent and the rent ascertained in accordance with schedule 9

6. All references to **"Rent"** will be changed to **"Yearly Rent"**

7. In clause 3 the Tenant will also covenant to observe and perform the obligations of the Tenant contained in schedule 9 (rent review)

8. In clause 4 the Landlord will also covenant to observe and perform the obligations of the Landlord contained in schedule 9 (rent review)

9. In clause 5 it will also be agreed and declared as set out in schedule 9 (rent review)

10. The following wording will be substituted for paragraph 7.1.2 of schedule 2:-

    "(unless and to the extent that the Landlord agrees otherwise) to reinstate and restore the Premises to the same state and condition as they were in prior to the carrying out of any works to the Premises whether such works were carried out during the Term; or prior to the Term during the term of years granted by the Previous Lease or under the agreement for the grant of such lease dated 15 June 2016 between Imperial College of Science Technology and Medicine (1) Convergence Pharmaceuticals Limited (2) and Biogen Idec Limited (3)"

11. The following wording will be inserted as a new paragraph 5 in schedule 7:-

"If on the commencement date of the new lease of the Premises granted pursuant to paragraph 4 of this schedule the Rental Value (as defined in schedule 9) has not been agreed or determined then the rent first reserved by such new lease will initially be equal to the Initial Rent payable under this Lease immediately prior to such Review Date (or if payment has been suspended or restricted the Yearly Rent which would have been payable had there been no suspension or restriction) but the second day of the term of such new lease will be an additional Review Date" A new schedule 9 will be inserted as follows:-

"Schedule 9

Rent Review

1. Rental Value

In this schedule **"Rental Value"** means the clear yearly rack rent at which the Premises might reasonably be expected to be let at the Review Date in the open market by a willing lessor to a willing lessee

1.1 assuming that:-

1.1.1 the Premises are to be let:-

(a) as a whole with vacant possession without any premium or other payment by the willing lessee

(b) for a term of five years from the Review Date

(c) otherwise on the same terms and conditions as are contained in this Lease (except as to the amount of the Yearly Rent but without provision for rent review and the definition of Permitted Use (which shall be modified in accordance with paragraph 1.1.2 below)

1.1.2 the Permitted Use under the Lease is any of the following:

(a) an open plan fully fitted Grade A office suite

(b) a Category A laboratory building, fully fitted out in accordance with the hypothetical tenant's requirements; or

(c) a combination of either of the descriptions at paragraphs (a) and (b) above

1.1.3 all the covenants contained in this Lease and the Previous Lease have been fully performed and observed

1.1.4 if the Premises or any means of access or egress or any Service Media have been destroyed or damaged or are being repaired they have been fully rebuilt and reinstated and repaired

1.1.5 the Premises may be lawfully used by the willing lessee for the use permitted by this Lease

1.1.6 the Premises are fully fitted out at the Landlord's option to:

(a) an open plan fully fitted Grade A office suite

(b) a Category A laboratory building, fully fitted out in accordance with the hypothetical tenant's requirements; or

(c) a combination of either of the descriptions at paragraphs (a) and (b) above

and are suitable and fit for immediate occupation and use by the willing lessee for the same use as has been assumed under paragraph 1.1.2 but the fit-out at the Premises is five years old on the Review Date

1.2 but disregarding:-

1.2.1 any effect on rent of the fact that the Tenant or any undertenant has been in occupation of the Premises or any part of them

1.2.2 any goodwill attached to the Premises by reason of the business then carried on at them by the Tenant or any undertenant

1.2.3 any effect on rent attributable to the existence of any lawful alteration or improvement to the Premises carried out during the Term (with the consent of the Landlord where required) or prior to the Term under the Previous Lease or an agreement for the grant of the Previous Lease by the Tenant or any undertenant or their respective predecessors in title (otherwise than pursuant to an obligation to the Landlord or its predecessors in title) and save to the extent that the Landlord has contributed to the cost of such alteration or improvement

1.2.4 so far as may be permitted by law any statutory prohibition or restriction relating to the assessment and recovery of rent

1.2.5 any work carried on at the Premises during or prior to the Term under an agreement for the grant of the Term by the Tenant or any undertenant or their respective predecessors in title which has diminished the rental value of the Premises

1.2.6 The provisions of this Schedule 9

2. Review

The Yearly Rent payable under this Lease will be reviewed on the Review Date and the Yearly Rent from and including the Review Date will be the higher of:-

2.1 £349,884.09; and

2.2 the Rental Value at the Review Date as agreed or determined in accordance with this schedule

3. Determination by surveyor

3.1 If the Landlord and the Tenant in the opinion of either of them are unable to agree the Rental Value of the Premises (whether or not an attempt to reach agreement has been made) then it will be determined at the request of either the Landlord or the Tenant

(made not earlier than three months prior to the expiry of the Previous Lease) by a chartered surveyor having current experience of rental values of property of a like kind and character to the Premises to be agreed upon by the Landlord and by the Tenant or at the request and option of either of them to be nominated by or on behalf of the President for the time being of the Royal Institution of Chartered Surveyors

3.2 Such surveyor will act as an arbitrator and in accordance with the Arbitration Act 1996 unless prior to his appointment as an arbitrator the Landlord and the Tenant agree that he should be appointed as an expert

3.3 If such surveyor is appointed as an expert:-

3.3.1 he will give notice to the Landlord and the Tenant inviting each of them to submit to him within such time as he stipulates a proposal for the Rental Value which may be supported by the submission of reasons and/or a professional valuation or report

3.3.2 he will afford to each party an opportunity to make counter-submissions in respect of any such submission valuation or report

3.3.3 he will give written reasons for his decisions

3.3.4 his fees and the costs of appointing him will be borne and paid by the Landlord and the Tenant in such shares and in such manner as he decides or failing such decision in equal shares

3.4 If any appointed surveyor dies or becomes unwilling to act or incapable of acting for any reason or fails to act with reasonable expedition another surveyor will be appointed in his place in like manner

4. Interim payments

4.1 If the Rental Value has not been agreed or determined by the Review Date the Initial Rent will continue to be payable until the Quarter Day next following the date of such agreement or determination; and

4.2 on such Quarter Day there will be due and payable to the Landlord by the Tenant:-

4.2.1 the Yearly Rent at the rate of the Rental Value so agreed or determined (the **"Reviewed Rent"**) due on such Quarter Day; and

4.2.2 a sum of money equal to the amount (if any) by which the Reviewed Rent exceeds the Initial Rent duly apportioned on a daily basis in respect of the period from the Review Date to such Quarter Day together with interest on it for the whole of such period calculated on a daily basis at a yearly rate equal to the Interest Rate

5. Statutory restrictions

If at the Review Date the Landlord is obliged to comply with any statute which restricts or modifies the Landlord's right to revise the Yearly Rent in accordance with the terms of this Lease or which restricts the right of the Landlord to demand or accept payment of the full amount of the Yearly Rent for the time being payable under this Lease then in each case respectively:

5.1 the operation of the provisions for such revision of the Yearly Rent will be postponed until the first day on which such operation may lawfully occur

5.2 the collection of any increase in the Yearly Rent will be postponed until the first date or dates upon which any such increase or any part of it may lawfully be collected.

6. Memorandum of reviewed rent

As soon as the amount of Yearly Rent payable after the Review Date has been agreed in accordance with the terms of this schedule the Landlord and the Tenant will if required by the Landlord without delay sign a memorandum of it

7. Time not of the essence

Time is not of the essence for the purposes of this schedule"

Executed as a deed by)

IMPERIAL COLLEGE THINKSPACE LIMITED)

on being signed by:) /s/ Eulian Roberts

/s/ Eulian Roberts) Director

in the presence of:)

Signature of witness: /s/ Katrina Lowther

Name: Katrina Lowther

Address: 66 Nantes Close

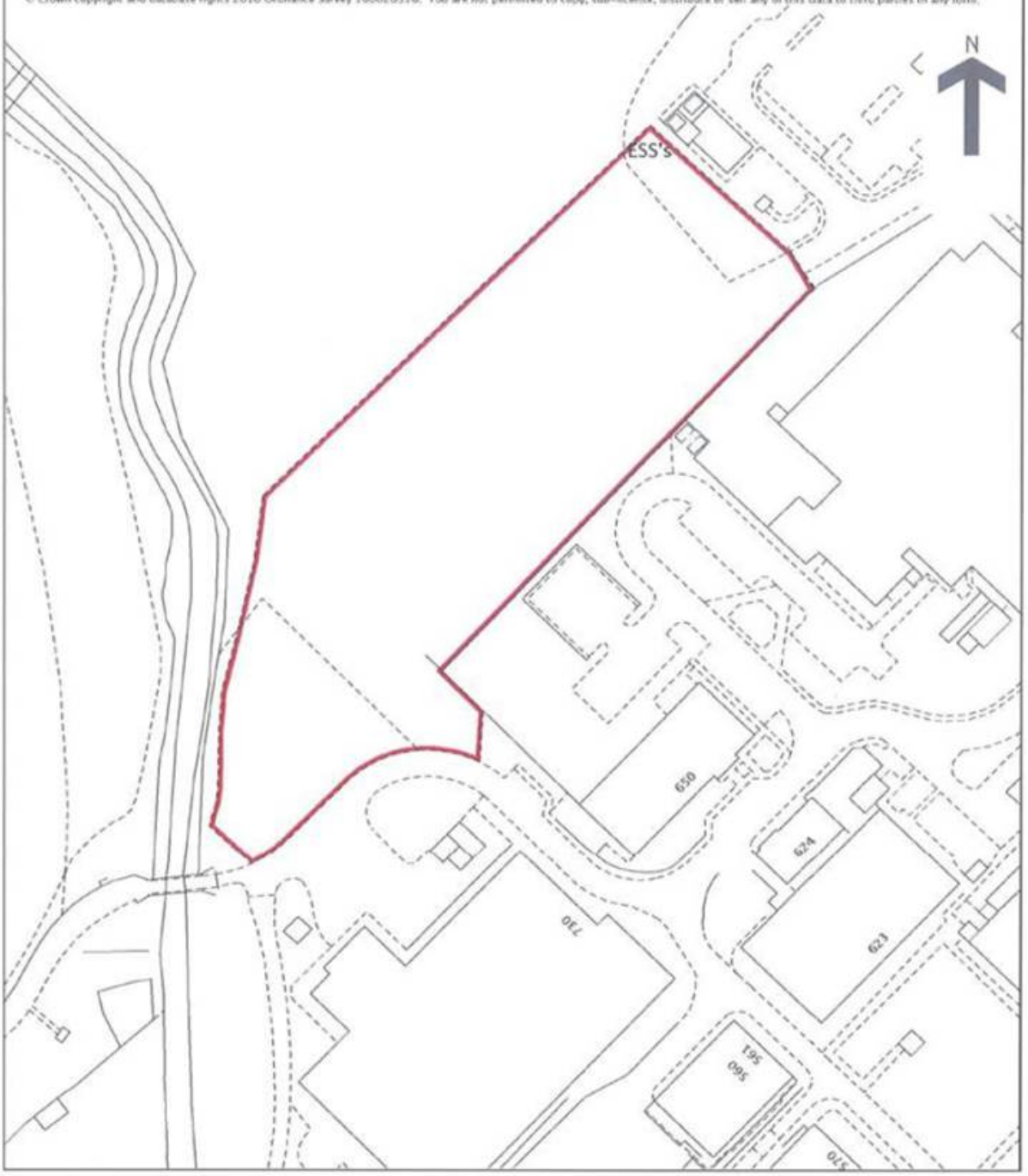
London SW18 1JL

Occupation: Executive Assistant

Plan A

Land Registry
Official copy of title plan

Title number **CB406367**
Ordnance Survey map reference **TL5050NE**
Scale **1:1250 enlarged from 1:2500**
Administrative area **Cambridgeshire : South Cambridgeshire**



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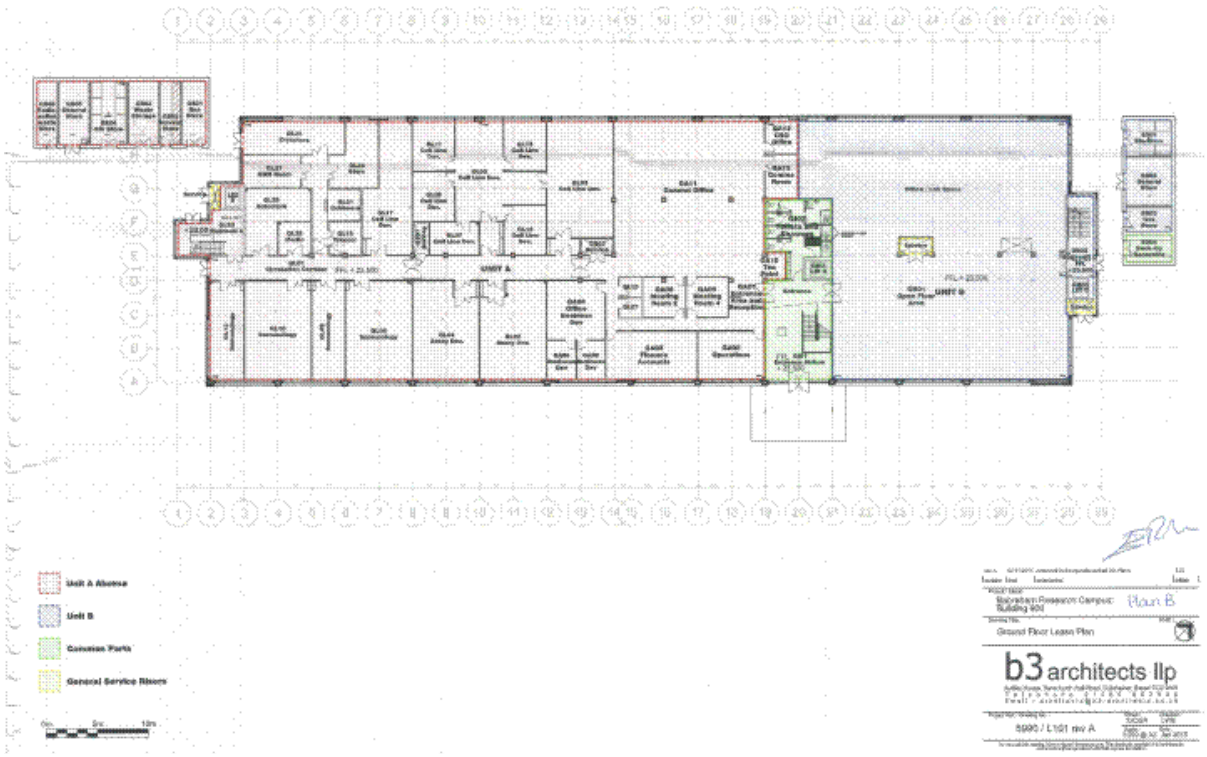


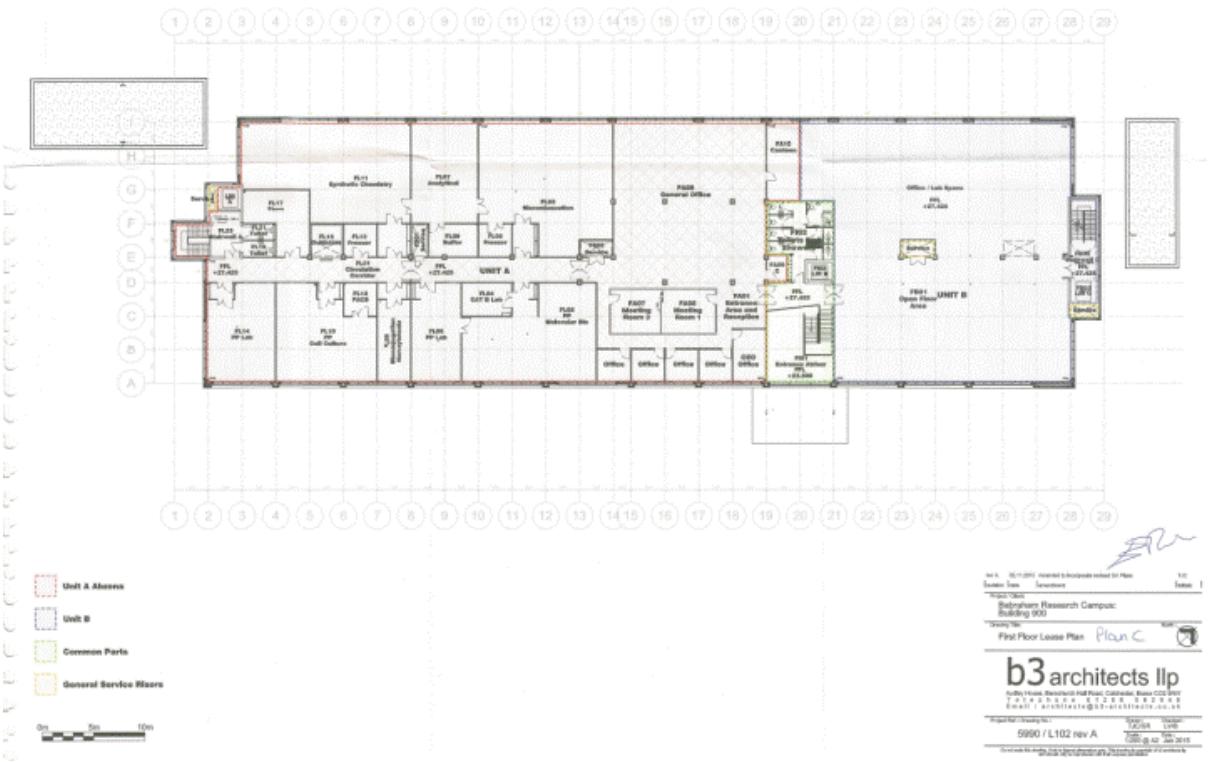
Babraham Research Campus:
Building 900

Plan B

Ground Floor Lease Plan

b3 architects llp

5990 / L101 rev A



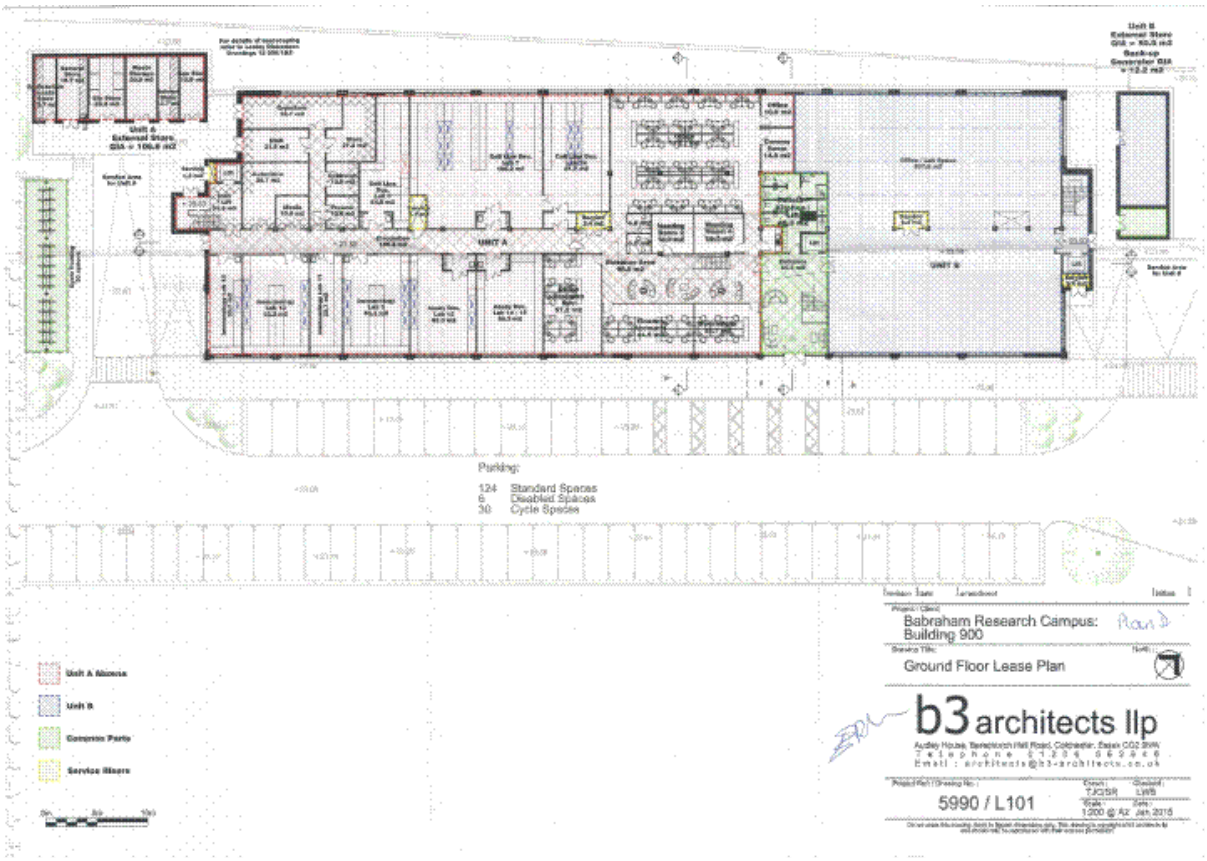
Babraham Research Campus:
Building 900

Plan C

First Floor Lease Plan

b3 architects llp

5990 / L102 rev A



DATED 31 OCTOBER 2017

CONTRACT FOR THE SALE OF LEASEHOLD LAND WITH VACANT POSSESSION

at

Ground and First Floor Premises Building 900, Babraham Research Campus, Babraham, Cambridge

between

Convergence Pharmaceuticals Limited

and

Bicycle RD Limited

This contract is dated 31 October 2017

Parties

(1) **CONVERGENCE PHARMACEUTICALS LIMITED** incorporated and registered in England and Wales with company number 09376285 whose registered office is at 70 Norden Road, Maidenhead, Berkshire, SL6 4AY (**Seller**)

(2) **BICYCLE RD LIMITED** incorporated and registered in England and Wales with company number 06960780 whose registered office is at Meditrina Building, Babraham Research Campus, Cambridge, CB22 3AT (**Buyer**)

1. Interpretation

The following definitions and rules of interpretation apply in this contract.

1.1 Definitions:

· **Buyer's Conveyancer**: Dechert LLP, 160 Queen Victoria Street, London, EC4 4QQ (Ref: D Gervais)

· **CAA 2001**: Capital Allowances Act 2001.

· **Equipment**: the equipment specified in Schedule 1.

· **Completion Date**: 31 October 2017

· **Consent**: a consent to the assignment to the Buyer of the residue of the term granted by the Lease.

· **Contract Rate**: interest at 2% per annum above the base rate from time to time of HSBC Bank Plc.

· **Deposit**: £ 1.00

· **Electronic Payment**: payment by electronic means in same day cleared funds from an account held in the name of the Buyer's Conveyancer at a clearing bank to an account in the name of the Seller's Conveyancer.

· **Landlord**: the person entitled to the immediate reversion to the Lease.

· **Lease**: the lease of the Property dated 2 March 2017 and made between Imperial College Thinkspace Limited (1) Convergence Pharmaceuticals Limited (2) and Biogen IDEC Limited (3) and every document varying or supplemental or collateral to it.

· **Part 1 Conditions**: the conditions in Part 1 of the Standard Commercial Property Conditions (Third Edition) and **Condition** means any one of them.

- **Part 2 Conditions**: the conditions in Part 2 of the Standard Commercial Property Conditions (Third Edition).
- **Property**: the leasehold property at Ground and First Floors Building 900, Babraham Research Campus, Babraham, Cambridge as demised by the Lease.
- **Purchase Price**: £350,000.00 plus VAT
- **Seller's Conveyancer**: Pitmans LLP, 107 Cheapside, London, EC2V 6DN (Ref: Bhaminee Sharma).
- **Superior Landlord**: the person entitled to the reversion (whether immediate or not) expectant on the determination of the term granted by a Superior Lease.
- **Superior Lease**: a lease which is superior to the Lease.
- **VAT**: value added tax chargeable in the UK.
- **Written Replies**: are:

    a) written replies that the Seller's Conveyancer has given prior to exchange of this agreement to any written enquiries raised by the Buyer's Conveyancer; or

    b) written replies to written enquiries given prior to exchange of this agreement by the Seller's Conveyancer to the Buyer's Conveyancer.

1.2 A **person** includes natural person, corporate or unincorporated body (whether or not having separate legal personality).

1.3 Unless otherwise specified, a reference to a statute or statutory provision is a reference to it as amended, extended or re-enacted from time to time and shall include all subordinate legislation made from time to time under that statute or statutory provision and all orders, notices, codes of practice and guidance made under it.

1.4 A reference to laws in general is a reference to all local, national and directly applicable supra-national laws as amended, extended or re-enacted from time to time and shall include all subordinate laws made from time to time under them and all orders, notices, codes of practice and guidance made under them.

1.5 The expression **tenant covenant** has the meaning given to it by the Landlord and Tenant (Covenants) Act 1995.

1.6 A reference to **writing** or **written** includes fax but not email.

1.7 Unless the context otherwise requires, references to clauses and Schedules are to the clauses and Schedules to this contract and references to paragraphs are to paragraphs of the relevant Schedule.

1.8 Clause, Schedule and paragraph headings shall not affect the interpretation of this contract.

1.9 The Schedules form part of this contract and shall have effect as if set out in full in the body of this contract. Any reference to this contract includes the Schedules.

1.10 Unless the context otherwise requires, words in the singular shall include the plural and in the plural shall include the singular.

1.11 Unless the context otherwise requires, a reference to one gender shall include a reference to the other genders.

1.12 Any obligation on a party not to do something includes an obligation not to allow that thing to be done.

1.13 For the purposes of the definition of Written Replies, **written replies** and **written enquiries** include any pre-contract enquiries and any replies to pre-contract enquiries that are requested or given by reference to the CPSE1 and CPSE4 enquiries and include enquiries or replies so requested or given by email.

2. Sale and purchase

2.1 The Seller will sell and the Buyer will buy the residue of the term of years granted by the Lease and the Equipment for the Purchase Price on the terms of this contract.

2.2 The Purchase Price will be apportioned:

(a) as to the residue of the Lease the sum of £ 1.00 and

(b) as to the Equipment the sum of £ 349,999.00.

2.3 The Buyer cannot require the Seller to:

(a) assign the Lease or any part of it to any person other than the Buyer; or

(b) assign the Lease in more than one parcel or by more than one transfer; or

(c) apportion the Purchase Price between different parts of the Property.

3. Conditions

3.1 The Part 1 Conditions are incorporated in this contract so far as they:

(a) apply to a sale by private treaty;

(b) relate to leasehold property;

(c) are not inconsistent with the other clauses in this contract; and

(d) have not been modified or excluded by any of the other clauses in this contract.

3.2 The terms used in this contract have the same meaning when used in the Part 1 Conditions.

3.3 The following Conditions are amended:

(a) Condition 1.1.1(d) is amended so that reference to the completion date in Condition 1.1.1(d) refers instead to the Completion Date as defined in this contract.

(b) Condition 1.1.1(e) is amended so that reference to the contract rate in Condition 1.1.1(e) refers instead to the Contract Rate as defined in this contract.

(c) Condition 1.1.1(o) is amended so that reference to VAT in Condition 1.1.1(o) refers instead to VAT as defined in this contract.

(d) Condition 7.6.3 is amended so that reference to “Condition 4.1.2” is reference to “Clause 9”.

3.4 Condition 1.1.4(a) does not apply to this contract.

3.5 The Part 2 Conditions are not incorporated into this contract.

4. Risk and insurance

4.1 With effect from exchange of this contract, the Property is at the Buyer’s risk and the Seller is under no obligation to the Buyer to insure the Property.

4.2 No damage to or destruction of the Property, nor any deterioration in its condition, however caused, will entitle the Buyer either to any reduction of the Purchase Price or to refuse to complete or to delay completion.

4.3 Conditions 8.2.2, 8.2.3 and 8.2.4(b) do not apply to this contract.

5. Deposit

5.1 On the date of this contract, the Buyer will pay the Deposit to the Seller’s Conveyancer as stakeholder on terms that on completion the Deposit is paid to the Seller with accrued interest.

5.2 The Deposit must be paid by Electronic Payment.

5.3 Conditions 3.2.1, 3.2.2 and 9.8.3 do not apply to this contract.

5.4 The provisions of clause 5.5, clause 5.6, clause 5.7 and clause 5.8 (inclusive) will only apply if:

(a) the Deposit is less than 10% of the Purchase Price; or

(b) no Deposit is payable on the date of this contract.

5.5 In this clause, the expression **Deposit Balance** means:

(a) (where the Deposit is less than 10% of the Purchase Price) the sum calculated by deducting the Deposit from 10% of the Purchase Price; or

(b) (where no Deposit is payable on the date of this contract) a sum equal to 10% of the Purchase Price.

5.6 If completion does not take place on the Completion Date due to the default of the Buyer, the Buyer will immediately pay to the Seller's Conveyancer the Deposit Balance (together with interest on it at the Contract Rate for the period from and including the Completion Date to and including the date of actual payment) by Electronic Payment.

5.7 After the Deposit Balance has been paid pursuant to clause 5.6, it will be treated as forming part of the Deposit for all purposes of this contract.

5.8 The provisions of clause 5.5, clause 5.6, and clause 5.7 (inclusive) are without prejudice to any other rights or remedies of the Seller in relation to any delay in completion.

6. Deducing title

6.1 The Seller's title to the Lease has been deduced to the Buyer's Conveyancer before the date of this contract.

6.2 The Buyer is deemed to have full knowledge of the title and is not entitled to raise any objection, enquiry or requisition in relation to it.

6.3 Conditions 7.1, 7.2, 7.3.1 and 7.4.2 do not apply to this contract.

7. Vacant possession

The Property will be sold with vacant possession on completion subject to the Equipment, which will remain in the Property.

8. Title guarantee

8.1 The Seller will assign the Lease with full title guarantee but the covenants implied by sections 3 and 4(1)(b) of the Law of Property (Miscellaneous Provisions) Act 1994 shall be limited so that the Seller will have no liability under them for the consequences of any breach of the terms of the Lease relating to the physical state or condition of the Property.

8.2 Condition 7.6.2 does not apply to this contract.

9. Matters affecting the Property

9.1 The Seller will assign the residue of the term of years granted by the Lease free from incumbrances other than:

(a) the tenant covenants and all terms and conditions contained or referred to in the Lease;

(b) any matters discoverable by inspection of the Property before the date of this contract;

(c) any matters which the Seller does not and could not reasonably know about;

(d) any matters disclosed or which would have been disclosed by the searches and enquiries which a prudent buyer would have made before entering into this contract;

(e) public requirements.

9.2 Conditions 4.1.1, 4.1.2 and 4.1.3 do not apply to this contract.

9.3 The Buyer is deemed to have full knowledge of the matters referred to in clause 9.1 and will not raise any enquiry, objection, requisition or claim in respect of any of them.

10. Consent

10.1 Completion is conditional on every Consent required under the Lease or any Superior Lease, being obtained on reasonable terms, each Consent being evidenced in a written, formal licence to assign, dated and signed or executed by or on behalf of each of the parties to it.

10.2 The Seller will apply for and use all reasonable endeavours to obtain every Consent as required by the Lease and any Superior Lease, but the Seller will not be obliged to seek any declaration of the Court that a Consent has been or is being unreasonably withheld.

10.3 The Buyer will, without delay:

(a) supply all reasonable and necessary information, accounts and references as the Landlord, any Superior Landlord or the Seller may reasonably require in connection with an application for or consideration of any Consent;

(b) ensure that any amendments that the Buyer proposes to make to any form of Consent or to any document mentioned in clause 10.3(c) that has been submitted to the Buyer or to the Buyer's Conveyancer, are communicated promptly to the Seller's Conveyancer;

(c) enter into a rental deposit with the Seller as security for the performance of the tenant covenants of the Lease; and

(d) execute the document containing a Consent and execute or procure the execution of the document required to be entered into pursuant to clause 10.3(c), each in the form reasonably required by the Landlord or by any Superior Landlord. The Buyer will return all such documents duly executed to the Seller's Conveyancer within five working days after the engrossment(s) have been submitted to the Buyer's Conveyancer.

10.4 If any Consent required under the Lease or any Superior Lease has not been obtained on reasonable terms by 4.00 pm on 24 November 2017 this contract may be rescinded:

(a) by the Seller giving notice to the Buyer; or

(b) by the Buyer giving notice to the Seller.

10.5 Without prejudice to Condition 10.2, if a notice to rescind is served under this clause, neither of the parties will have any further rights or obligations under this contract except that:

(a) the Buyer will continue to be liable to pay or refund any costs that the Buyer is liable to pay or refund under this contract;

(b) the Seller's rights in connection with any breach of this contract by the Buyer which may have occurred before service of the notice to rescind will be unaffected;

10.6 Condition 11.3 does not apply to this contract.

11. Assignment

11.1 The assignment to the Buyer will be in the agreed form annexed to this contract.

11.2 The Buyer and the Seller will execute the assignment in original and counterpart.

11.3 Condition 7.6.5(b) does not apply to this contract.

12. VAT

12.1 Each amount stated to be payable by the Buyer to the Seller under or pursuant to this contract is exclusive of VAT (if any).

12.2 If any VAT is chargeable on any supply made by the Seller under or pursuant to this contract, the Buyer will on receipt of a valid VAT invoice, pay the Seller an amount equal to that VAT as additional consideration on completion.

12.3 Conditions 2.1 and 2.2 do not apply to this contract.

13. Completion

13.1 Completion will take place on the Completion Date or, if later, on the date which is five working days after every Consent has been obtained in accordance with clause 10 but time is not of the essence of the contract unless a notice to complete has been served.

13.2 Condition 9.1.1 does not apply to this contract.

13.3 Condition 9.4 is amended to add, "(d) any other sum which the parties agree under the terms of the contract should be paid or allowed on completion".

13.4 Condition 9.7 is amended to read: "The buyer is to pay the money due on completion by Electronic Payment and, if appropriate, by an unconditional release of a deposit held by a stakeholder".

14. Apportionment of rent payable under the Lease

14.1 In this clause the following definitions apply:

- **Lease Rent**: the annual rent first reserved by the Lease excluding any VAT paid in respect of it.
- **Lease Rent Payment Day**: a day under the Lease for payment of the Lease Rent or an instalment of the Lease Rent.

14.2 The Lease Rent will be apportioned so that on completion the Buyer will pay or allow the Seller:

(A x B)/365

where:

A is the Lease Rent payable at the date of completion; and

B is the number of days from and including the day of completion to but excluding the next Lease Rent Payment Day.

15. Service charge and insurance due under the Lease

15.1 The Service Charge and Estate Service Charge (as defined in and payable under the Lease) will be apportioned in accordance with Condition 9.3. The Seller will remain liable for and will indemnify the Buyer in respect of any balancing payments of Service Charge or Estate Service Charge or any costs associated with the provision of any additional services provided to the Seller under the Lease which are levied on the Buyer by the Landlord and which relate to a period prior to the Completion Date.

15.2 The Buyer hereby agrees to repay to the Seller as soon as reasonably practicable any sums received from the Landlord by way of reimbursement for any overpayment of Service Charge and Estate Service Charge made by the Seller during their period of ownership following final reconciliation of the Service Charge and Estate Service Charge by the Landlord and the Superior Landlord at the end of the current service charge year

15.3 To the extent that the Insurance Rent (as defined in the Lease) does not form part of the Service Charge the Insurance Rent shall be apportioned in accordance with Condition 9.3 and the Seller will remain liable for any Insurance Rent due in respect of its period of ownership and shall promptly indemnify the Buyer in respect of any such sums charged to the Buyer.

16. Business rates

The Seller will remain liable for any business rates payable in respect of its period of ownership of the Property and will promptly indemnify the Buyer in respect of any such sums charged to the Buyer by the local rating authority.

17. Capital allowances election

The Seller and the Buyer shall, on Completion, make a joint election under section 198 of the CAA 2001 in accordance with the provisions of Schedule 2 of this agreement.(2)

18. Buyer's acknowledgement of condition

The Buyer acknowledges that before the date of this contract, the Seller has given the Buyer and others authorised by the Buyer, permission and the opportunity to inspect, survey and carry out investigations as to the condition of the Property. The Buyer has

formed the Buyer's own view as to the condition of the Property and the suitability of the Property for the Buyer's purposes.

19. Entire agreement

19.1 This contract constitutes the whole agreement between the parties and supersedes all previous discussions, correspondence, negotiations, arrangements, understandings and agreements between them relating to its subject matter

19.2 The Buyer acknowledges that in entering into this contract the Buyer does not rely on, and shall have no remedies in respect of, any representation or warranty (whether made innocently or negligently) other than those:

(a) set out in this contract]; or

(b) contained in any Written Replies.

19.3 Nothing in this clause shall limit or exclude any liability for fraud.

19.4 Condition 10.1 is varied to read, "If any plan or statement in the contract, or in Written Replies, is or was misleading or inaccurate due to an error or omission the remedies available are as follows."

20. Notices

20.1 Any notice given under this contract must be in writing and signed by or on behalf of the party giving it.

20.2 Any notice or document to be given or delivered under this contract must be:

(a) delivered by hand; or

(b) sent by pre-paid first class post or other next working day delivery service; or

(c) sent through the document exchange (DX); or

(d) sent by fax.

20.3 Any notice or document to be given or delivered under this contract must be sent to the relevant party as follows:

(a) to the Seller at:

70 Norden Road, Maidenhead, Berkshire SL6 4AY

marked for the attention of: Rajita Sharma

or at the Seller's Conveyancer, quoting the reference Bhaminee Sharma

(b) to the Buyer at:

Meditrina Building, Babraham Research Campus, Cambridge, CB22 3AT

marked for the attention of: Kevin Leee

or at the Buyer's Conveyancer, quoting the reference 961267/157280

or as otherwise specified by the relevant party by notice in writing to the other party.

20.4 Any change of the details in clause 20.3 specified in accordance with that clause shall take effect for the party notified of the change at 9.00 am on the later of:

(a) the date, if any, specified in the notice as the effective date for the change; or

(b) the date five working days after deemed receipt of the notice.

20.5 Giving or delivering a notice or a document to a party's conveyancer has the same effect as giving or delivering it to that party.

20.6 Any notice or document given or delivered in accordance with clause 20.1, clause 20.2 and clause 20.3 will be deemed to have been received:

(a) if delivered by hand, on signature of a delivery receipt or at the time the notice or document is left at the address provided that if delivery occurs before 9.00 am on a working day, the notice will be deemed to have been received at 9.00 am on that day, and if delivery occurs after 5.00 pm on a working day, or on a day which is not a working day, the notice will be deemed to have been received at 9.00 am on the next working day; or

(b) if sent by pre-paid first class post or other next working day delivery service, at 9.00 am on the working day after posting ; or

(c) if sent through the DX, at 9.00 am on the second working day after being put into the DX ; or

(d) if sent by fax, at the time of transmission provided that if transmission occurs before 9.00 am on a working day, the notice or document will be deemed to have been received at 9.00 am on that day, and if transmission occurs after 5.00 pm on a working day, or on a day which is not a working day, the notice will be deemed to have been received at 9.00 am on the next working day.

20.7 In proving delivery of a notice or document, it will be sufficient to prove that:

(a) a delivery receipt was signed or that the notice or document was left at the address; or

(b) the envelope containing the notice or document was properly addressed and posted by pre-paid first class post or other next working day delivery service; or

(c) the envelope containing the notice or document was properly addressed and was put in the DX; or

(d) the fax was properly addressed and transmitted.

20.8 A notice or document given or delivered under this contract shall not be validly given or delivered if sent by email.

20.9 Condition 1.3 does not apply to this contract.

20.10 This clause does not apply to the service of any proceedings or other documents in any legal action or, where applicable, any arbitration or other method of dispute resolution.

21. Warranties

21.1 On or, in the case of the 4 see Risk Management warranty, as soon as reasonably possible after completion the Seller shall assign the benefit of the following warranties to the Buyer:-

De Grey Management limited (as Certifying Officer) dated 31 October 2017;
B3 – Architect dated 31 October 2017
TWS – Structural Engineer dated 31 October 2017
MLM – M&E Engineer dated 31 October 2017
4See Risk Management – CDM Co-ordinator to be completed
Hutton Construction Limited dated 31 October 2017

22. Third party rights

22.1 A person who is not a party to this contract shall not have any rights under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this contract.

22.2 Condition 1.5 does not apply to this contract.

23. Governing law

This contract and any dispute or claim arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

24. Jurisdiction

Each party irrevocably agrees that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this contract or its subject matter or formation (including non-contractual disputes or claims).

This contract has been entered into on the date stated at the beginning of it.

Schedule 1 Equipment

400 MHz Bruker NMR;
3 Biotage automated purifyers;
1 Waters Xevo LCMS;
1 Agilent HPLC;
1 Agilent preparative HPLC;
1 Agilent LCMS;
1 Julabo Chiller;
1 Huber Chiller;
An Asynt large scale reactor with two vessels;
an ozonizer;
a Buckingham and Stanley polarimeter;
a Parr hydrogenation apparatus;
a vaccum oven.
Ice machine
Autoclaves
Glasswash

Schedule 2 Capital allowances election

Part 1 Making of an election

1. The following definitions apply in this Schedule 2.

   Election: a capital allowances election pursuant to section 198 of the CAA 2001.

   Elected Figure: the value of the Fixed Plant in accordance with the apportionment set out in the Election.

   Fixed Plant: such plant and machinery (within the meaning of CAA 2001) as constitutes a fixture or fixtures on which the Seller is, or will be, required to bring a disposal value into account on the sale of the Property as detailed in the Election.

2. On Completion, the Seller and the Buyer shall sign in respect of the Property in duplicate the Election agreeing to the Elected Figure, being the disposal value for the Fixed Plant required to be brought into account by the Seller and falling to be treated as expenditure incurred by the Buyer on the provision of the Fixed Plant.

3. The Seller and the Buyer shall each submit the Election in the form set out in Part 2 of this Schedule 2 to HM Revenue & Customs within the time limit prescribed by law and take all reasonable steps to procure that the Elected Figure is accepted by HM Revenue & Customs.

4. The Seller and the Buyer agree to reflect the Elected Figure in their respective tax (capital allowances) computations and returns.

5. To enable the Buyer to make and substantiate claims under CAA 2001 in respect of the Property, the Seller shall use its reasonable endeavours to provide, or to procure that its agents provide:

   (a) copies of all relevant information in its possession or that of its agents; and

   (b) such cooperation and assistance as the Buyer may reasonably require.

6. The Buyer agrees that:

   (a) it will only use such information as is provided pursuant to paragraph 5 for the stated purpose; and

   (b) it will not disclose, without the consent of the Seller, any such information which the Seller expressly provides on a confidential basis.

7. If for any reason the Election, or the notification of it, is deficient, ineffective or otherwise not accepted by HM Revenue & Customs, the Seller and the Buyer shall each take all reasonable steps necessary to obtain the agreement of HM Revenue & Customs to

the apportionment specified in the Election for the purposes of capital allowances including making any amendments to the Election or the signing of a replacement election (in either case, to the extent possible).

Part 2 Notice of an election to use an alternative apportionment in accordance with section 198 of the Capital Allowances Act 2001

Property address:	Ground & First Floor Premises Building 900, Babraham Research Campus, Babraham, Cambridge
Interest:	Leasehold
Title number:	N/A
Seller's name and address:	Convergence Pharmaceuticals Limited, 70 Norden Road, Maidenhead, Berkshire SL6 4AY
Seller's Unique Taxpayer Reference Number:	9213911910
Buyer's name and address:	Bicycle RD Limited, Meditrina Building, Babraham Research Campus, Cambridge CB22 3AT
Buyer's Unique Taxpayer Reference Number:	4680725770
Date of completion of sale:	
Amount apportioned to machinery and plant fixtures in the Seller's special rate pool:	Nil
Amount apportioned to machinery and plant fixtures in the Seller's main pool:	£ 349,999.00
Sale price:	£ 350,000.00

The Seller and the Buyer hereby jointly and severally elect pursuant to the provisions of section 198 of the CAA 2001 that the amount which, for all purposes of Part 2 of the CAA 2001, is to be taken as the portion of the sale price of the interest specified above which falls to be included as expenditure incurred by the Buyer on the provision of plant and machinery fixtures is £ 349,999.00. A list of the fixtures and the amount to be apportioned to them is set out below.

Integral features and other plant and machinery fixtures in the special rate pool

Items	Apportioned amount Integral features (for the Seller) and other plant and machinery fixtures allocated to the special rate pool (£)
Electrical systems (including lighting systems)	
Cold water systems	
Space or water heating systems, powered systems of ventilation, air cooling or air purification, and any floor or ceiling comprised of such systems	
Lifts, escalators and moving walkways	
External solar shading (i.e. brise soleil)	
TOTAL	Nil

Integral features and other plant and machinery fixtures in the main pool

Items	Apportioned amount Integral features (for the Seller) and other plant and machinery fixtures allocated to the main pool (£)	
Electrical systems (including lighting systems)		
Cold water systems		
Space or water heating systems, powered systems of ventilation, air cooling or air purification, and any floor or ceiling comprised of such systems		
Lifts, escalators and moving walkways		
External solar shading (i.e. brise soleil)		
Laboratory Equipment	£	349,999.00
TOTAL	£	349,999.00

Signed by

for and on behalf of
CONVERGENCE PHARMACEUTICALS LIMITED

Director

Signed by

for and on behalf of
BICYCLE RD LIMITED

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the use in Amendment No. 1 to this Registration Statement on Form S-1 of Bicycle Therapeutics Limited of our report dated March 22, 2019, except for the effects of the corporate reorganization by way of a bonus share issuance having the effect of a share split as described in Note 1 to the consolidated financial statements, as to which the date is May 13, 2019 relating to the financial statements of Bicycle Therapeutics Limited, which appears in this Registration Statement. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP
Cambridge, United Kingdom
May 13, 2019

QuickLinks

Exhibit 99.1

Consent of Director Nominee

Bicycle Therapeutics Limited is filing a Registration Statement on Form S-1 with the Securities and Exchange Commission under the Securities Act of 1933, as amended (the "Securities Act"), in connection with the initial public offering of American Depositary Shares. In connection therewith, I hereby consent, pursuant to Rule 438 of the Securities Act, to being named as a nominee to the board of Bicycle Therapeutics Limited in the Registration Statement, as may be amended from time to time. I also consent to the filing of this consent as an exhibit to such Registration Statement and any amendments thereto.

/s/ Bosun Hua
Name: Bosun Hua
Date: May 13, 2019