UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2019.

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number 001-38916

BICYCLE THERAPEUTICS PLC
(Exact name of registrant as specified in its charter)

England and Wales (State or Other Jurisdiction of Incorporation or Organization)	**Not Applicable** (I.R.S. Employer Identification No.)
B900, Babraham Research Campus **Cambridge, United Kingdom** (Address of Principal Executive Offices)	**CB22 3AT** (Zip Code)

Registrant's telephone number, including area code **+44 1223 261503**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value £0.01 per share*	n/a	The Nasdaq Stock Market LLC
American Depositary Shares, each representing one ordinary share, nominal value £0.01 per share	BCYC	The Nasdaq Stock Market LLC

* Not for trading, but only in connection with the listing of the American Depositary Shares on the NASDAQ Global Select Market.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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 ☐ Accelerated filer ☐ Non-accelerated filer ☐ 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. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value (approximate) of the registrant's voting and non-voting common equity held by non-affiliates based on the closing price per American Depositary Share, or ADS, of the registrant's ADSs on The Nasdaq Global Select Market on June 30, 2019 (the last business day of the registrant's most recently completed second fiscal quarter) was $114,461,603.

As of March 5, 2020, the registrant had 17,994,772 ordinary shares, nominal value £0.01 per share, outstanding.

Documents Incorporated by Reference:

Portions of the registrant's definitive proxy statement, or Proxy Statement, for its 2020 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2019, are incorporated by reference into Part III of this Annual Report on Form 10-K.

SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS.

This Annual Report on Form 10-K contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by such forward-looking terminology as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Any forward-looking statement involves known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by such forward-looking statement. Forward-looking statements include statements, other than statements of historical fact, about, among other things:

- 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 *Bicycle* Toxin Conjugate ("BTC"), tumor-targeted immune cell agonist programs, 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 Jumpstart Our Business Startups Act ("JOBS Act");
- statements regarding future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, these statements are based on our estimates or projections of the future that are subject to known and unknown risks and uncertainties and other important factors that may cause our actual results, level of activity, performance, experience or achievements to differ materially from those expressed or implied by any forward-looking statement. These risks, uncertainties and other factors are described in greater detail under the caption "Risk Factors" in Part I. Item 1A and elsewhere in this Annual Report on Form 10-K. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur. Undue reliance should not be placed on any forward-looking statement.

In addition, any forward-looking statement in this Annual Report represents our views only as of the date of this annual report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, except as required by applicable law. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

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PART I

ITEM 1. BUSINESS.

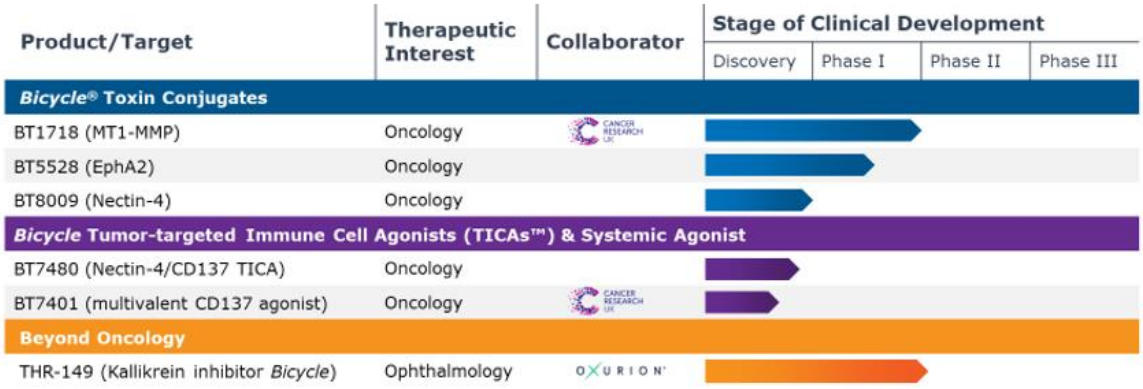
We are a clinical-stage biopharmaceutical company developing a novel and differentiated class of medicines, which we refer to as *Bicycles*®, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint is designed to confer high affinity and selectivity, making *Bicycles* attractive candidates for drug development. *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. The relatively large surface area presented by *Bicycles* allow targets to be drugged that have historically been intractable to non-biological approaches. *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 are also evaluating BT5528, a second-generation BTC targeting Ephrin type-A receptor 2, or EphA2, in a Company-sponsored Phase I/II study and are conducting Investigational New Drug application, or IND, -enabling activities for BT8009, a BTC targeting Nectin-4. Our discovery pipeline in oncology includes *Bicycle*-based systemic immune cell agonists and *Bicycle* tumor-targeted immune cell agonists (TICAs™).

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, ophthalmology and respiratory indications.

The following table summarizes key information about our programs:



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*. From our founding through December 31, 2019, we have generated substantial intellectual property, including four patent families directed to novel scaffolds, 16 patent families directed to our platform technology, 69 patent families directed to bicyclic peptides and related conjugates, and seven 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.

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:

- ***Progress our most advanced candidates, BT1718 and BT5528, through clinical development.*** BT1718 is being investigated in an ongoing Phase I/IIa clinical trial sponsored by CRUK. We intend to advance development of this candidate aggressively across oncology indications in which the target MT1-MMP is expressed. We expect CRUK to initiate expansion cohorts in the Phase IIa portion of the Phase I/IIa study in 2020. Bicycle is also evaluating BT5528 in an ongoing company-sponsored Phase I/II trial in patients with solid tumors.

- ***Advance BT8009 into clinical development.*** We intend to progress our IND-enabling activities for BT8009 to advance this program into clinical development for oncology indications in 2020. Based on promising observations from our preclinical models, we believe Nectin-4 is an attractive target for cytotoxin delivery and that *Bicycles* provide a promising delivery modality.

- ***Continue IND-enabling activities for our lead TICA program, BT7480.*** BT7480 is a *Bicycle* tumor-targeted immune cell agonist (TICA) targeting Nectin-4 and agonizing CD137. The constrained nature of *Bicycles* confers high affinity and selectivity and enables us to link tumor targeting *Bicycles* to *Bicycles* that agonize CD137, providing tumor-specific effects. In preclinical experiments with BT7480, we have

observed that these characteristics promote powerful anti-tumor activity. We expect to progress our IND-enabling activities for BT7480 in 2020.

- ***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 systemic and tumor-targeted immune cell agonists, from which we expect to identify additional development candidates.

- ***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 and immune cell agonists, 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, 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.

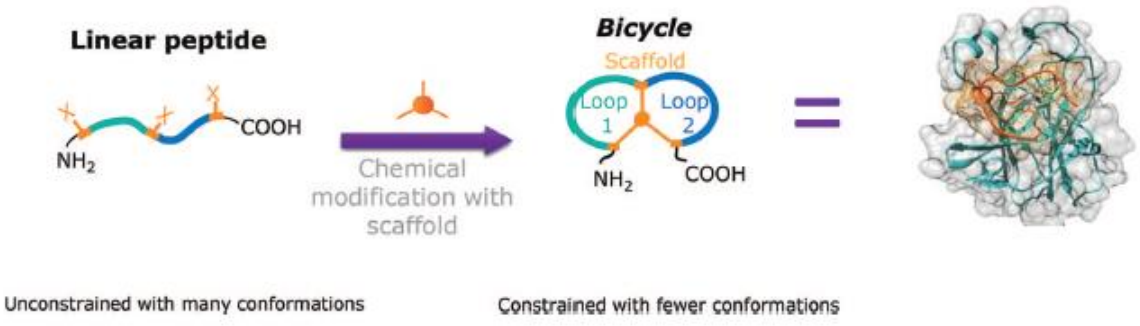
The *Bicycle* Opportunity

Introduction to Bicycles

Bicycles are fully synthetic, short peptides consisting of nine to 20 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^{20} today. We have applied our novel *Bicycle* modality to a growing range of targets, from a single target in 2009 to more than 105 today. We can create a wide range of *Bicycles* by varying four parameters:

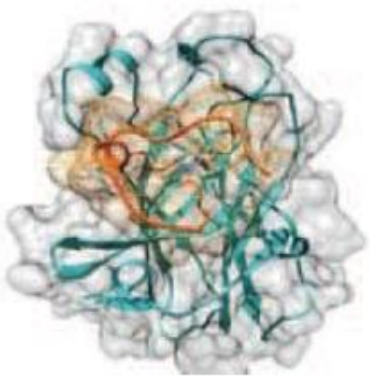
- the number of amino acids in the two loops;
- the amino acid composition at each position;
- the symmetry of the two loops; and
- the small molecule scaffold used to cyclize the *Bicycle*.

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

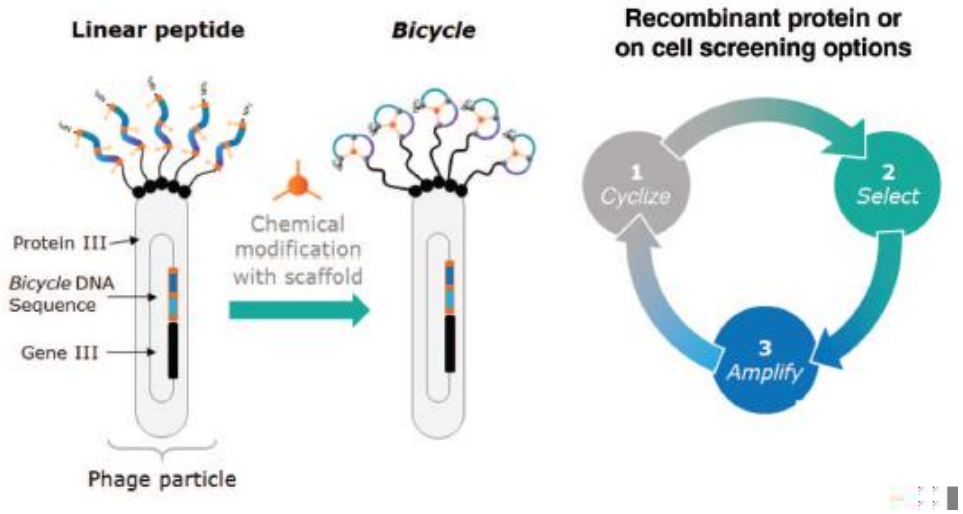
We utilize our novel and proprietary phage display screening platform to identify *Bicycles* that are potentially useful in medicine. We have used this technology to identify our current pipeline, and intend to leverage it to develop a broader portfolio of product candidates to address unmet medical 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 agonists 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 systemic and tumor-targeted immune cell agonist programs. 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 105 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
BT5528	• High EphA2 expressing tumors (e.g., lung cancer, breast cancer, bladder cancer, gastric cancer, ovarian cancer, esophageal cancer, pancreatic cancer)	• Phase I/IIa	• Ongoing company-sponsored Phase I/IIa clinical trial
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 **Tumor-targeted Immune Cell Agonists (TICAS™) and Systemic Agonists**			
BT7480 (Nectin-4/CD137 TICA)	• Oncology	• Preclinical	• IND-enabling activities in process
BT7401 (multivalent CD137 agonist)	• Oncology	• Preclinical	• CRUK to fund and sponsor development through a Phase IIa clinical study
EphA2/CD137 TICA	• 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
Novel anti-bacterials	• Anti-bacterials	• Discovery	• Collaborating with Innovate UK and Small Business Research Initiative
Neurological	• Dementia	• Discovery	• Collaborating with Dementia Discovery Fund and Oxford Drug Discovery Institute

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 cell agonists. 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 tumor-targeted 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 are evaluating BT5528, our first second-generation BTC that targets EphA2 and carries a monomethyl auristatin E, or MMAE, cytotoxin payload, in an ongoing, company-sponsored Phase I/IIa clinical trial to assess safety, tolerability and efficacy in patients with solid tumors. We are conducting IND-enabling activities for BT8009, a BTC that targets Nectin-4 and also carries an MMAE cytotoxin payload. 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. Clinical data from three post-dose tumor biopsies in patients from our ongoing Phase I/IIa 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 for at least 120 hours after dosing. Preliminary clinical data observed to date from our ongoing Phase I/IIa 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.

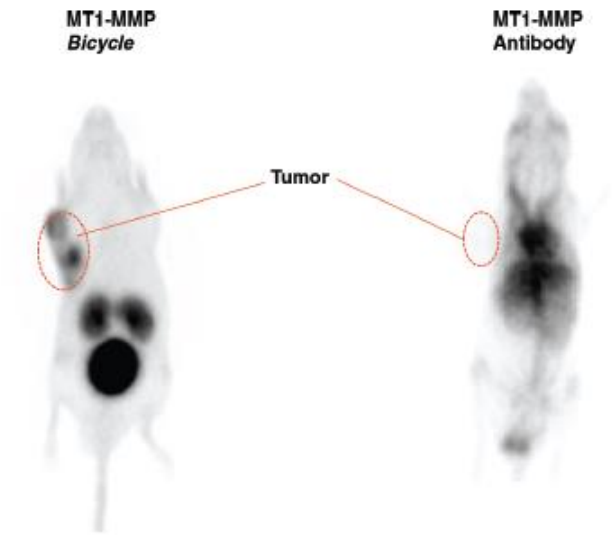
- ***Larger toxin payload.*** Despite the small size of *Bicycles*, they are able to carry a larger dose of toxin per unit mass than a comparator ADC. Therefore, we believe that *Bicycles* can deliver a higher concentration of the linked toxin to increase the probability of tumor killing.

- ***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.

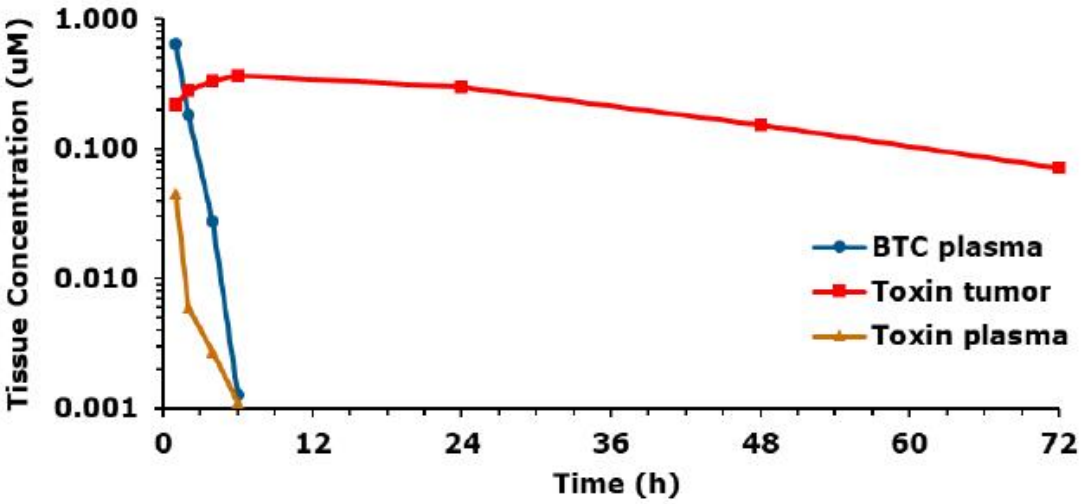
PET Imaging Revealing Payload Delivery in a Mouse Model



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

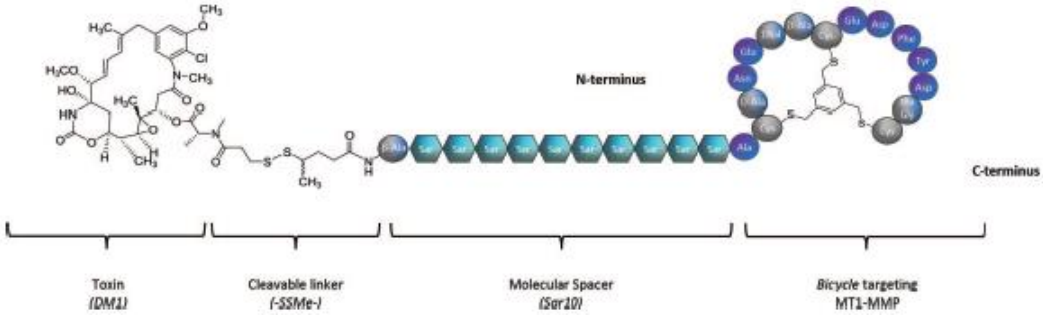


We believe these data demonstrate the potential of BTCs to have long-term sustained activity and to limit the toxicity that is associated with ADCs.

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

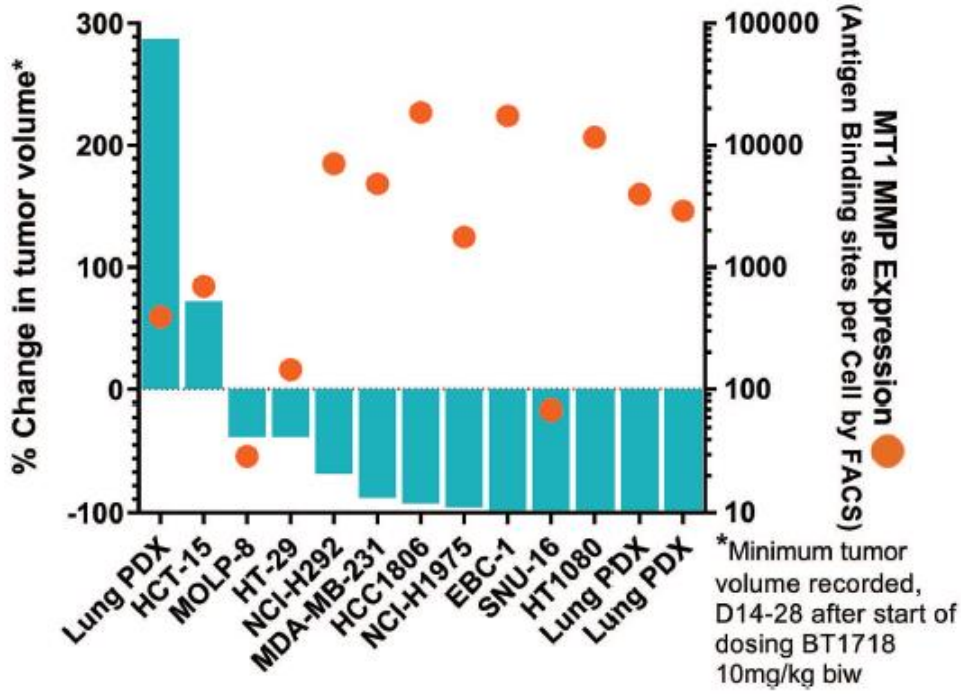


MT1-MMP is a matrix metalloprotease involved in tissue remodeling and is generally expressed at relatively low levels in normal adult tissues. MT1-MMP has an established role in cell invasion and metastasis, and we believe that MT1-MMP is an attractive target for cytotoxin delivery due to its high level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

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.

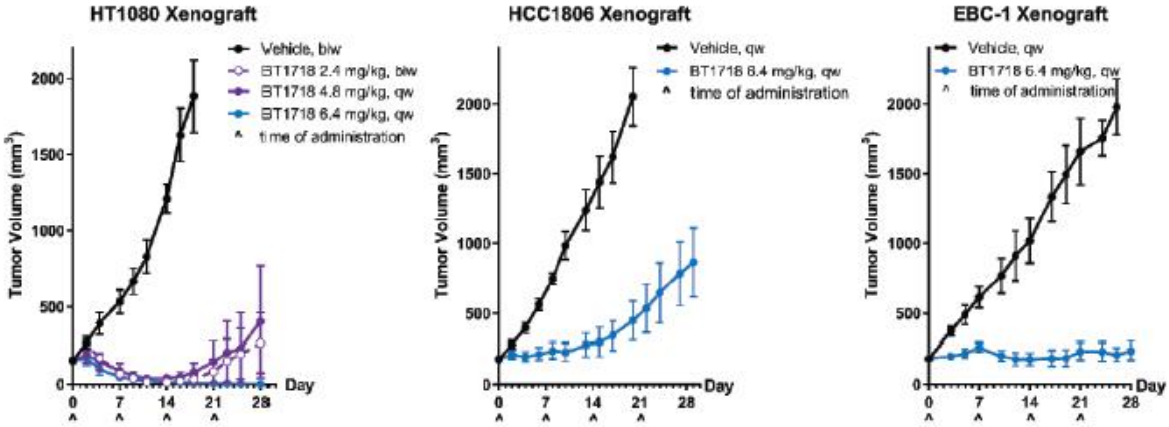
Preclinical Experience

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

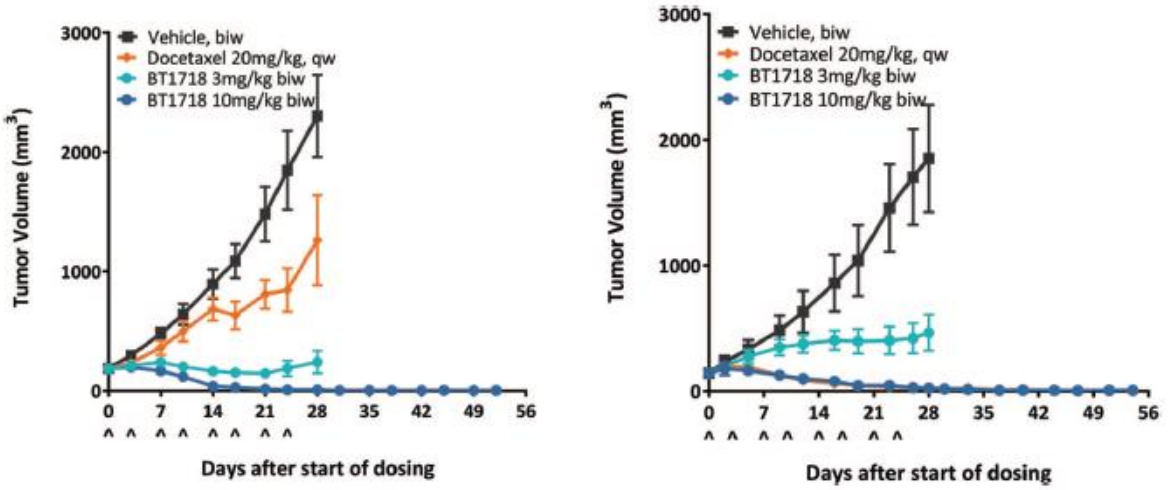
Mouse Dose (mg/kg)	Human Equivalent Dose (mg/m^2)
2.4	7.2
3.0	9.0
4.8	14.4
6.4	19.2
10.0	30.0

Effect of Administration of BT1718 in Cell Line Derived Xenograft Models



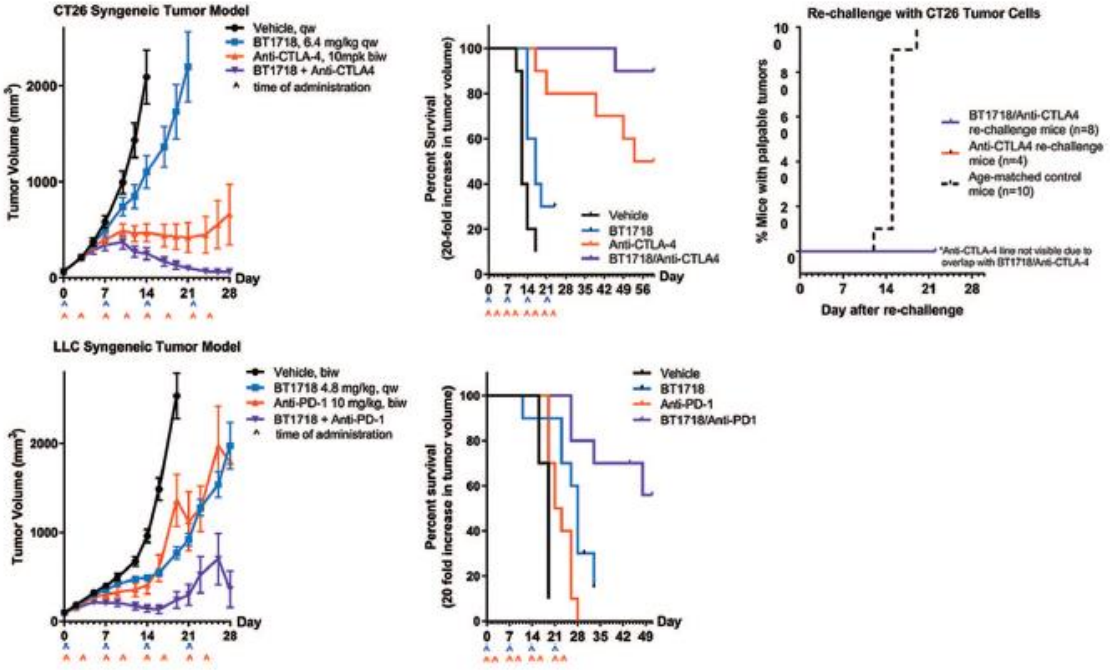
Patient-derived xenograft, or PDX, models are designed to capture patient responses to oncology therapy in a heterogeneous cohort of patients with solid tumors with 80-100% correlation between the PDX and patient response. BT1718 was also evaluated in two lung adenocarcinoma PDX models, one sensitive 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. The Phase I part of this trial evaluates up to 40 patients with advanced solid tumors in two dosing regimens at three sites in the United Kingdom.

The Phase I part of this clinical trial evaluates the safety and tolerability of BT1718 in patients with advanced solid tumors, regardless of tumor MT1-MMP expression levels, and establishes a recommended Phase II dose. The Phase I part of the trial has evaluated 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 are being explored.

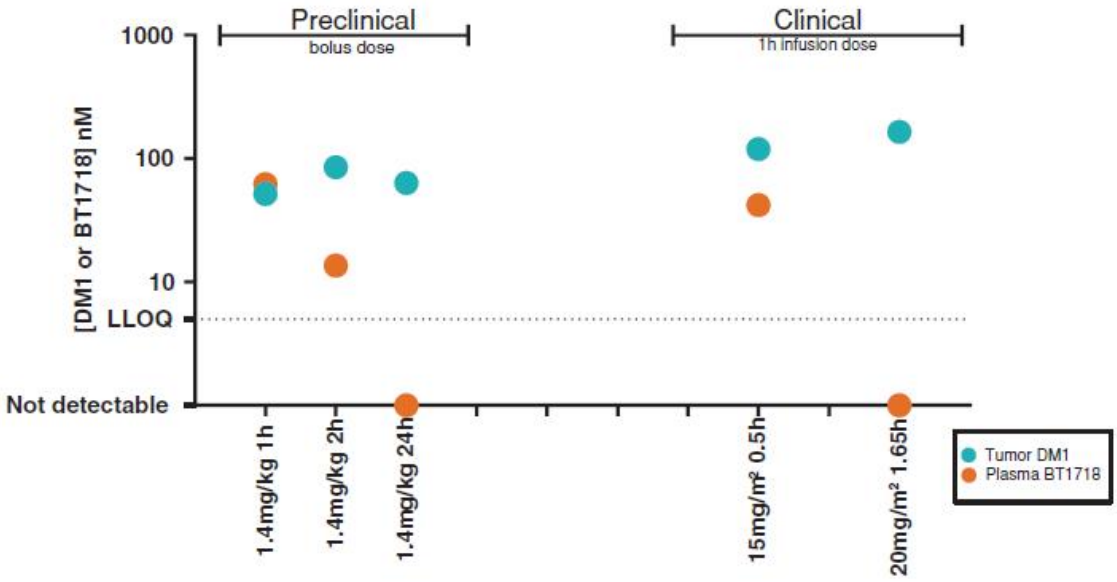
The Phase IIa part of the trial will evaluate BT1718 in patients with tumors that express MT1-MMP at the recommended Phase II dose based on the findings from the Phase I part of the trial. We will determine tumor types for investigation in this part of the trial in conjunction with CRUK. To determine 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.

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 or fresh 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. 15 patients across six cohorts have been dosed and evaluated on the twice-weekly schedule, with doses ranging from 0.6 mg/m^2 to 9.6 mg/m^2. As of February 13, 2020, 24 patients across five cohorts have been dosed and evaluated in the once-weekly schedule with doses ranging from 9.6 mg/m^2 to 32 mg/m^2. With once-weekly dosing, which is the expected schedule for the Phase IIa portion of the study, BT1718 has appeared generally tolerable, with generally manageable adverse events at doses believed to be in the therapeutic range based on preclinical data. We expect CRUK to initiate expansion cohorts in the Phase IIa portion of the Phase I/IIa study in 2020.

DM1 delivery has been demonstrated in tumor biopsies at early timepoints (2 out of 3 patients). Concentrations of DM1 in the clinical tumor biopsy samples are consistent with preclinical data obtained at doses that gave partial (4.2 mg/m2) and full (14.4 mg/m2) tumor regression in mouse xenograft models. In the phase IIa part of the study, additional tumor biopsies will be taken at later timepoints to further evaluate DM1 retention.

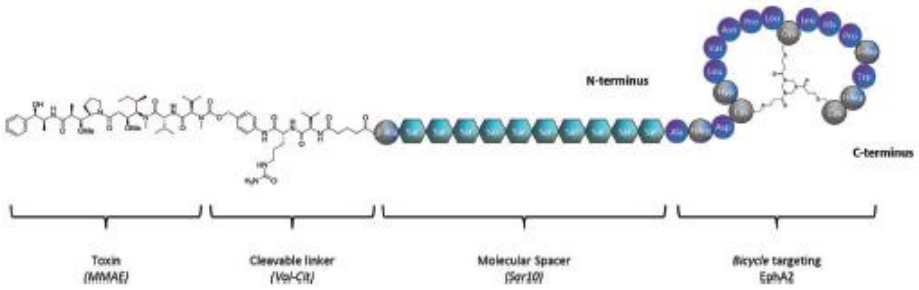
DM1 Levels in Clinical and Preclinical Tumor Samples



BT5528

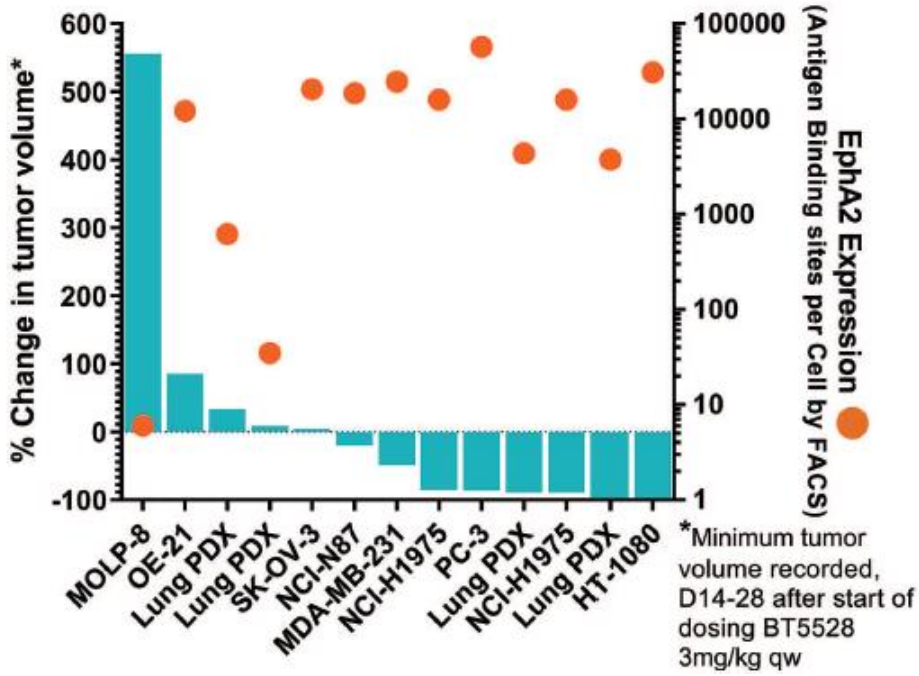
BT5528 is a BTC designed to target EphA2. The molecule is comprised of our EphA2 targeting *Bicycle*, a valine-citrulline, or val-cit, cleavable linker and a cytotoxin MMAE payload.

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.

Preclinical Experience

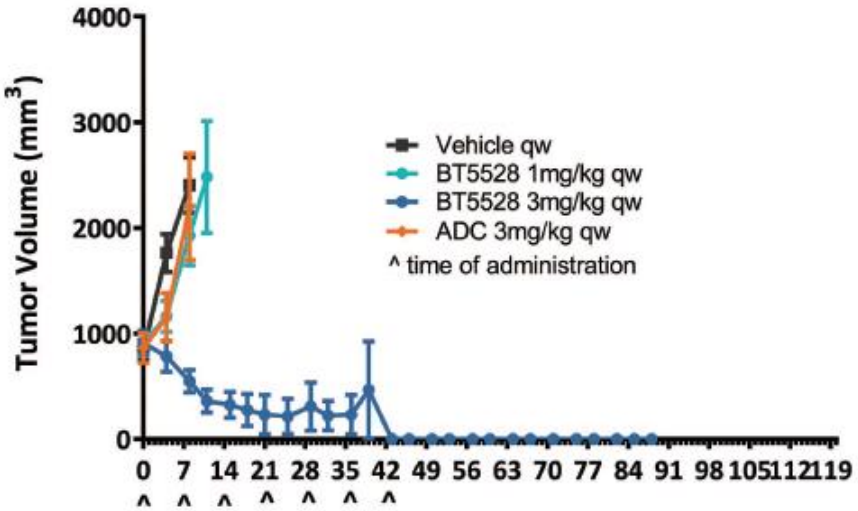
BT5528 has been evaluated in preclinical studies in multiple species, including rodents and non-human primates. In our preclinical studies, BT5528 was not observed to have a significant effect on clotting parameters and did not exhibit abnormal liver function at tolerated doses. We also observed no bleeding 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.

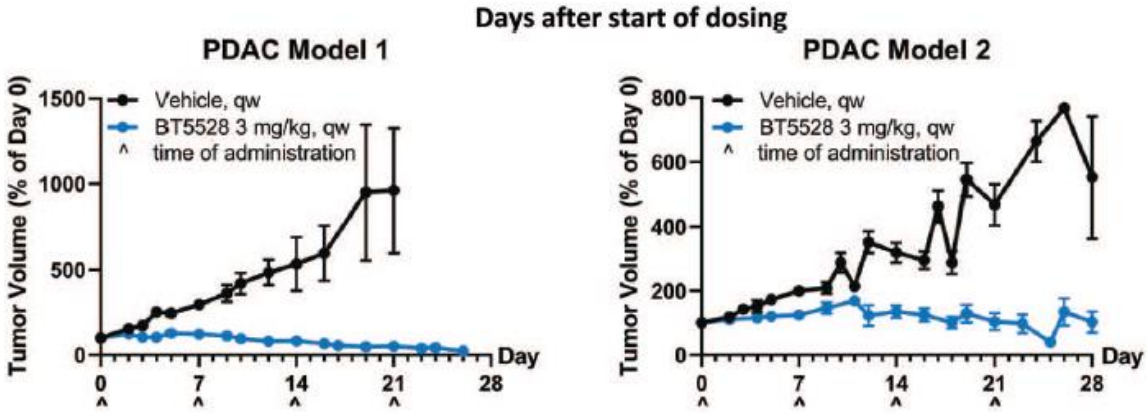
In *in vivo* preclinical studies, we observed dose-dependent anti-tumor activity following administration of BT5528 with disease stabilization or regression in multiple xenograft models representing tumor types including lung, breast, gastric, fibrosarcoma, prostate, ovarian and esophageal, with activity 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

Docetaxel resistant NSCLC model





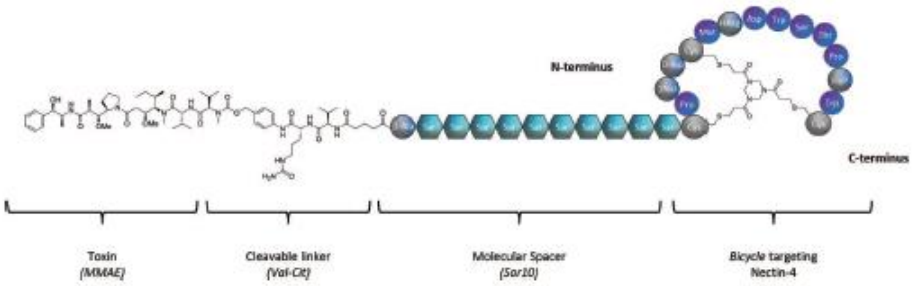
Clinical Development

In November 2019, Bicycle announced that the first patient had been dosed in the Phase I dose escalation portion of a Company-sponsored Phase I/II clinical trial of BT5528 in patients with advanced solid tumors associated with EphA2 expression. The Phase I/II multi-center, open-label trial will evaluate BT5528 administered once-weekly as a single agent and in combination with nivolumab. The Phase I portion is a dose escalation primarily designed to assess the safety and tolerability of BT5528 and to determine a recommended Phase II dose. Following selection of a recommended Phase II dose, a Phase II dose expansion portion will be initiated with the primary objective of evaluating the clinical activity of BT5528. The study will be conducted across sites in the U.S. and the UK. The Phase I dose escalation remains 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.

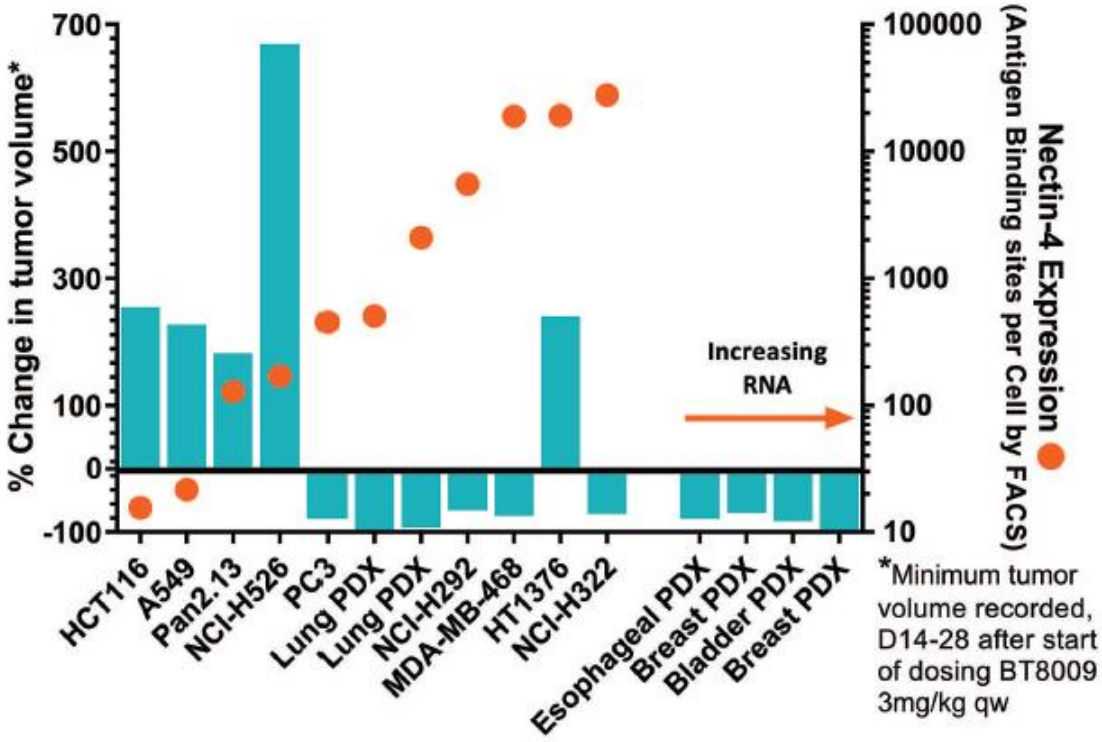
Schematic of BT8009



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, enfortumab vedotin, which is being jointly conducted by Seattle Genetics and Astellas and, in December 2019, received approval from the U.S. Food and Drug Administration (FDA) as a treatment for patients with locally advanced or metastatic urothelial cancer following treatment with platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor. 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.

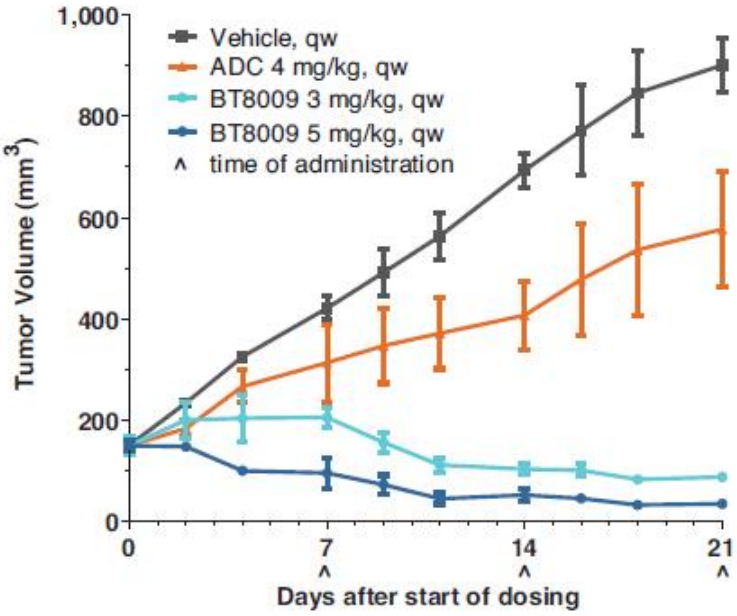
Preclinical Experience

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, BT8009 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 time points 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 a decrease in tumor volume.

Effect of BT8009 on Tumor Volume in a Preclinical Non-Small Cell Lung Cancer-Derived Xenograft Model



Bicycle *Immune Cell Agonist*

Approaches that activate cytotoxic T-cells and other types of cells 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.

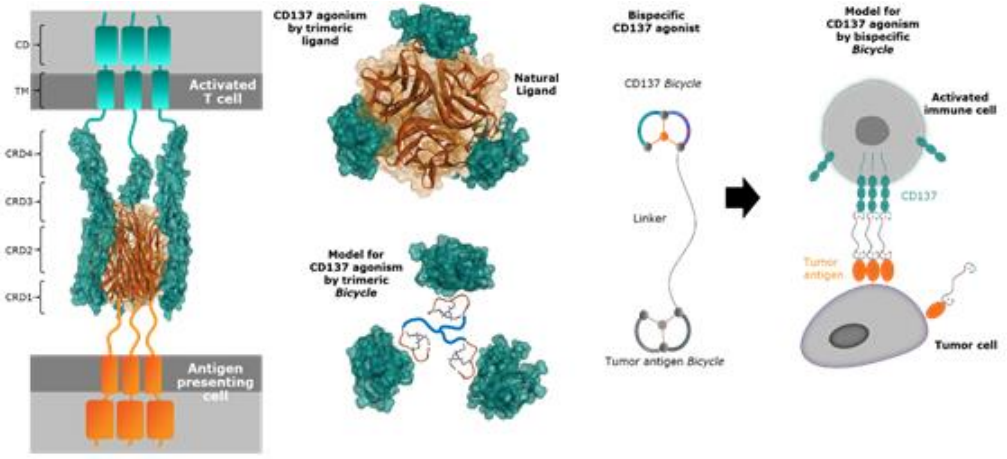
We are aware of anti-CD137 antibodies undergoing clinical testing, including urelumab being developed by Bristol-Myers Squibb, which produced single agent responses but also severe liver toxicity, and utomilumab being developed by Pfizer, which exhibited minimal clinical activity with less toxicity. We are developing immune cell agonists, designed to trigger an immune response to tumors. We have identified potent *Bicycle* agonists of CD137, 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 small size and PK characteristics of *Bicycles*. Our *Bicycle* immune cell agonists are designed to circumvent the limitations of antibody and biologic therapies, such as liver toxicity and limited efficacy, and to better enable combination therapy. *Bicycle* immune cell agonists can be formed by conjugating multiple copies of a CD137 *Bicycle* to form multimers or by utilizing a bi-specific format in which CD137 *Bicycles* are linked to *Bicycles* that bind to tumor antigens, inhibit checkpoint proteins or otherwise activate the immune system. We believe we are currently the only company that has fully chemically synthetic multivalent or tumor-targeted CD137 agonists.

Properties of Bicycle *Immune Cell Agonists*

In order to agonize the CD137 receptor, cross-linking of a trimeric receptor is required. As a result, we are developing multivalent systemic and tumor-targeted molecules that cross-link the receptor into an active form in a tumor cell independent or dependent manner as shown in the image below.

Schematic of Proposed CD137* Bicycle *Agonists



These *Bicycle* CD137 agonists 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 systemic and tumor-targeted immune cell agonizing *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 multivalent and tumor-targeted *Bicycles* are in the range of approximately 4 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 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 and in combination with other Bicycles 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.

- ***Tumor targeting***. Combining CD137-binding *Bicycles* with *Bicycles* that bind to tumor targets potentially affords an additional level of safety as compared to systemically active agonists such as urelumab. The clustering and activation of CD137 occurs only when the tumor-targeting *Bicycle* binds to both the tumor antigen target and CD137. Therefore, we expect the tumor targeted agonists will achieve a higher degree of activation locally in the tumor but will have significantly reduced or no activity in healthy tissues that do not express the tumor antigen.

Comparison of the Features of our Bicycle Immune Cell Agonists to Biological Immune 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 multivalent; ~3.5-8 kDa for tumor-targeted immune cell agonists (TICAS) • Linkage through various sites of attachment allows presentation of binder in various orientations • Easy to make tri- and tetrameric molecules • Immunogenicity unlikely—multivalent 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

Multivalent CD137 Immune Cell Agonists

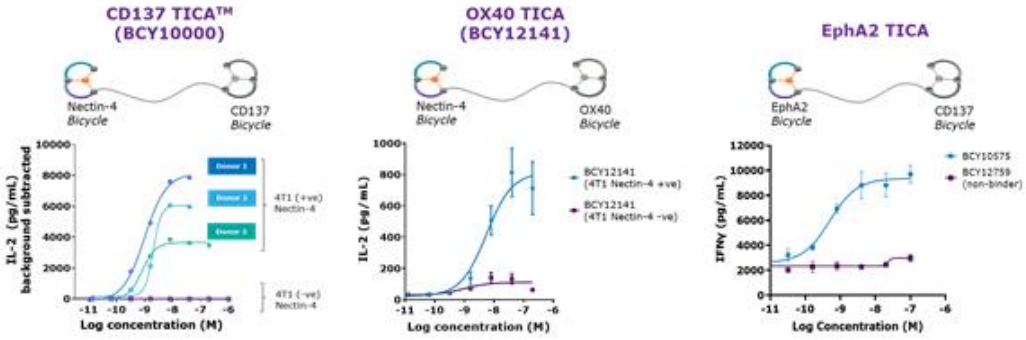
We observed that simple multivalent *Bicycle* CD137 agonists displayed potent activity in preclinical cell-based assays. Several *Bicycle* CD137 agonists displayed comparable or higher fold induction compared to the natural ligand (CD137L) in an engineered reporter cell assay whereby CD137 activation leads to production of a luminescence signal. We also observed *Bicycles* stimulated the release of the cytokine IL-2, a marker of immune response, from primary human T-cells. In additional *in vivo* studies, we observed that CD137-binding *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.

Bicycle *Tumor-Targeted Immune Cell Agonists (TICAs)*

We have linked immune cell receptor binding *Bicycles* to tumor antigen binding *Bicycles* to form TICAs. We have found this approach to be generalizable across tumor antigen and immune cell receptors. We constructed CD137-targeting TICA molecules and observed that these bi-specific *Bicycles* agonize the CD137 receptor only in the presence of cells that express the appropriate tumor antigen. Additionally, we have constructed TICA molecules with *Bicycles* that bind to another member of the TNF family of T-cell costimulatory receptors TNFRSF4, also known as OX40. As shown in the figure below, TICA molecules combining our Nectin-4 or EphA2 tumor antigen binding *Bicycles* and CD137 or OX40 binding *Bicycles* stimulated the release of the cytokine IL-2 or IFN from human PBMCs when in co-culture with tumor cells that express appropriate receptor (Nectin-4 or EphA2). In co-culture with cells lacking Nectin-4

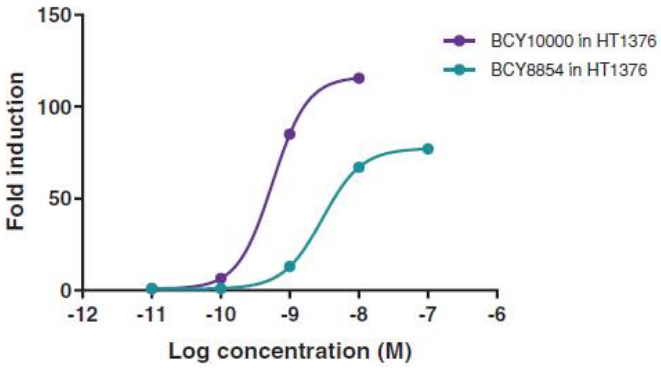
expression, or when non-binding *Bicycles* are incorporated (such as BCY12759) there was no activity observed. This is an example of how both the immune cell binding and tumor cell binding *Bicycles* can be readily interchanged in the context of our synthetic TICA molecules to generate novel and targeted immune agonists for further study.

Modularity of TICAs



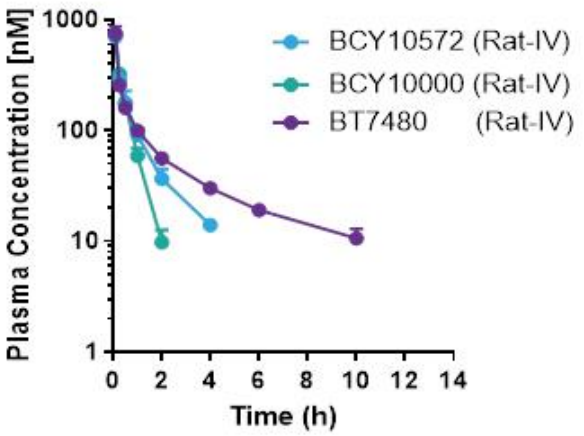
In our preclinical development of TICA molecules, we have observed an ability to tune molecules based on simple chemical changes, which we believe is an inherent advantage of our *Bicycle* platform-based approach to bi-specifics compared to other modalities. As an example of this, activity of two different Nectin-4/CD137 TICA 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 CD137 TICAs



We also observed that the pharmacokinetic properties of TICA molecules can be tuned through chemical changes. The figure below shows the plasma concentrations over time of three Nectin-4/CD137 TICA molecules after i.v. infusion into rats at a dose of 3 mg/kg. BCY11863 demonstrates a longer circulation time than BCY10000 and BCY10572. This data shows that the properties of the TICAs can be modulated to extend the duration of exposure in vivo.

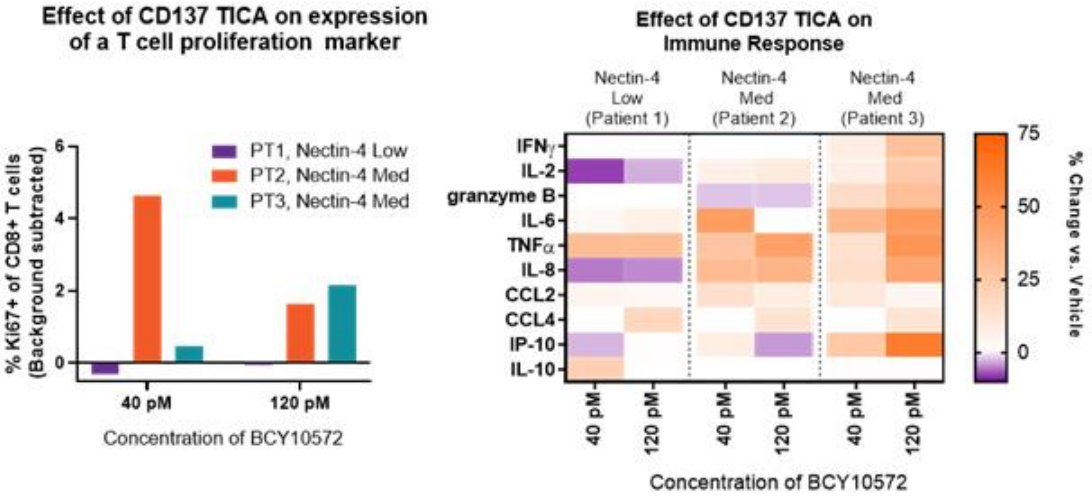
Tunable Pharmacokinetics of CD137 TICAs



In additional studies, we observed that a tumor-targeted Nectin-4/CD137 agonist 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.

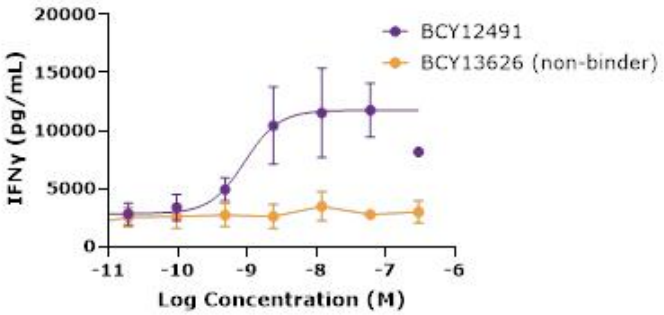
CD137 and Nectin-4 Expression in Patient Samples

	CD137+ T cells (%)	Nectin-4+ cells (%)
Patient 1	19.8	4.4
Patient 2	15.1	25.8
Patient 3	30.0	15.1



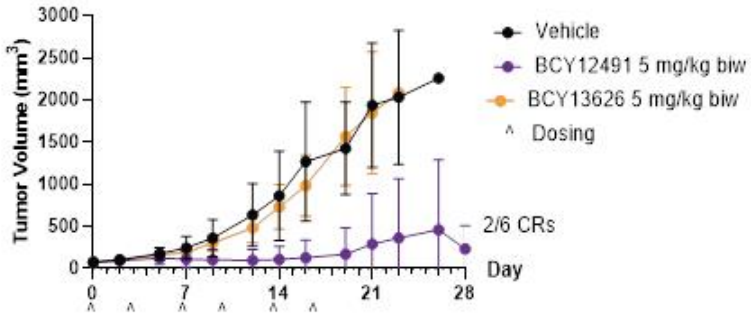
As shown in the figure below, we have also observed that an EphA2/CD137 TICA, BCY12491, is capable of eliciting high levels of pro-inflammatory cytokine interferon gamma when incubated with human derived PBMCs in the presence of MC38 tumor cells expressing EphA2, while a non-binding control molecule, BCY13626, exhibits no activity.

***Activity of EphA2 TICA* in vitro**



In further studies, we have observed that intermittent dosing of BCY12491 leads to a robust anti-tumor activity in syngeneic MC38 mouse model using humanized CD137 (huCD137) C57BL/6 mice. Administration of BCY12491 in six intravenous biweekly doses over a period of 17 days at 5 mg/kg lead to substantial tumor regressions, including two out of six complete responses (CRs). In addition, administration of BCY13626, a non-binding analog of BCY12491 had no impact on tumor growth rates.

***Activity of EphA2 TICA* in vivo**

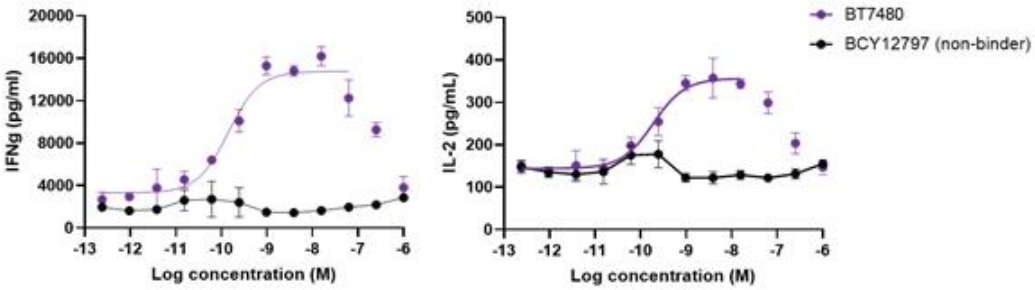


We believe that our ability to rapidly generate and test TICA molecules and their simple molecular format may form the basis of additional programs in the future. In addition to the immune cell and tumor targets that we have already investigated, we are also planning to screen for, or have started to screen for, *Bicycles* that target the NK cell receptors FcgRIIIA and NKp46 as well as additional immune cell and tumor specific antigens.

BT7480

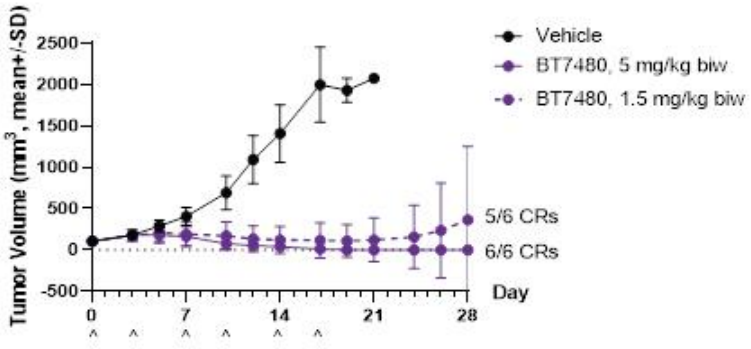
BT7480 is a TICA that targets CD137 and Nectin-4. BT7480 exhibits potent CD137 agonism in an engineered CD137 reporter assay system that correlates with Nectin-4 surface expression on the co-cultured tumor cells. In addition, BT7480 induces robust production of interleukin-2 (IL-2) and interferon gamma (IFNg) in primary PBMC/tumor cell co-culture assays. This activity is strictly dependent on the tumor cells expressing Nectin-4 and on the ability of the TICA to bind to both of its targets, Nectin-4 and CD137. In the figure below, BT7480 induces IL-2 and IFN at sub nanomolar concentrations when incubated with human PBMCs and the Nectin-4 expressing human tumor cell line HT1376.

BT7480 produces IL-2 and IFN*g *in coculture with PBMC and HT1376



Additionally, we have observed that intermittent dosing of BT7480 leads to a robust anti-tumor activity in syngeneic MC38 mouse model, engineered to overexpress Nectin-4, using humanized CD137 (huCD137) C57BL/6 mice. Administration of BT7480 in six intravenous biweekly doses over a period of 17 days at 1.5 or 5 mg/kg lead to substantial tumor regressions, including five out of six complete responses at 1.5 mg/kg and six out of six complete responses at 5 mg/kg (CRs). In addition, animals that were complete responders in the experiment were subsequently re-challenged with the same tumor cell implantation and no tumor growth was observed, implying development of immunogenic memory.

Effect of BT7480 on Tumor Volume in a Preclinical Syngeneic Model with Nectin-4 Expressing MC38 Tumors in C57BL/6 Mice



Our IND-enabling preclinical studies for BT7480 are currently ongoing.

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.

Sanofi (formerly Bioverativ). In August 2017, we entered into a collaboration agreement with Bioverativ, Inc., (which was acquired by Sanofi in March 2018, or Sanofi), in the field of non-malignant hematology, including hemophilia. This collaboration was terminated during 2019.

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 was completed in July 2019. The Phase I clinical trial, conducted by Oxurion, was an open-label, multi-center, non-randomized study to evaluate the safety of a single intravitreal injection of THR-149 at three ascending dose levels in 12 subjects with visual impairment due to center-involved DME. The study also investigated changes to patients' best corrected visual acuity (BCVA). A rapid onset of action was observed from Day 1, with an increasing average improvement in BCVA of up to 7.5 letters at Day 14. This activity was maintained with an average improvement in BCVA of 6.5 letters at Day 90 following a single injection of THR-149.

Our Collaborations

Cancer Research UK

BT1718

In December 2016, we entered into a clinical trial and license agreement with 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, Cancer Research Technology Limited may elect to receive 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 I 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.

BT7401

In December 2019, we entered into a clinical trial and license agreement with Cancer Research Technology Limited and CRUK. Pursuant to the agreement, CRUK's Centre for Drug Development will fund and sponsor development of BT7401 from current preclinical studies through the completion of a Phase IIa trial in patients with advanced solid tumors.

We granted to CRUK a license to our intellectual property in order for CRUK to design, prepare for, sponsor, and carry out the clinical trial and all necessary preclinical activities to support the trial. We retain the right to continue the development of BT7401 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 contain BT7401 or all the pharmaceutically active parts of BT7401, 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 55% to 80% of the net revenue depending on the stage of development when the license is granted) less certain costs, as defined in the agreement. The CRUK agreement contains additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash, with an aggregate total value of up to $60.3 million for each licensed product, as well as royalty payments based on a single digit percentage on net sales of

products developed, and sublicense royalties to the CRUK in the low double digit percentage of sublicense income depending on the stage of development when the license is granted.

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 upon written notice by either party prior to the last cycle of treatment has been completed under the clinical trial. If the study is terminated by us prior to the filing of a clinical trial authorization, or by the CRUK for an insolvency event or a material breach by us prior to the start of a clinical trial, we will reimburse CRUK for certain costs paid or committed prior to the start of the clinical trial. 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. DDF is a specialized venture capital fund focused on discovering and developing novel therapies for dementia. In October 2019, the collaboration with DDF was expanded to include Oxford University's Oxford Drug Discovery Institute (ODDI). Under the terms of the agreement, Bicycle and DDF will collaborate to identify *Bicycles* that bind to clinically validated dementia targets. ODDI will then profile these *Bicycles* in a range of target-specific and disease-focused assays to assess their therapeutic potential. If promising lead compounds are identified, DDF, ODDI 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.

Sanofi (formerly Bioverativ)

In August 2017, we entered into a research collaboration agreement with Bioverativ Inc., which was acquired by Sanofi in March 2018, or Sanofi, in the field of non-malignant hematology. The Sanofi collaboration agreement targeted two disease areas, with an option to add a third. We used our Bicycle screening platform to perform research and development services for the programs and Sanofi could select, under one or more license collaborations, products for each program.

Under the Sanofi agreement, we were 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) consisted of two stages. The first was an initial stage of screening and optimization to identify high affinity *Bicycle* binders and optimization of early drug like properties and was led by Bicycle. If lead compounds were identified, the second stage included chemical optimization and testing of these compounds in disease relevant biological assays, conducted jointly by us and Sanofi, in preparation for lead collaboration product nomination. Each collaboration program had a maximum initial period of three years, unless a program was abandoned or extended for up to one year by Sanofi. Sanofi could, 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 have paid 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. Sanofi would lead preclinical and clinical development, as well as subsequent marketing and commercialization.

Under the terms of the Sanofi collaboration agreement, we granted to Sanofi, 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 Sanofi 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 Sanofi 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 Sanofi 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, Sanofi 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, Sanofi was 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, Sanofi 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 were also eligible to receive up to $104.0 million in regulatory milestone payments for each collaboration product. In addition, we were 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 Sanofi were 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 Sanofi faces generic competition in certain countries.

Either party could 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 continued after the specified cure period. Either party could 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 could be terminated by either party in its entirety, or, if the breach was limited to a country or countries, with respect to the country or countries to which the breach applies. Sanofi may terminate the agreement, entirely or on a program by program, licensed product by licensed product or country by country basis, for convenience.

Sanofi 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. Sanofi exercised its right to terminate the sickle cell program in March 2019. Effective October 23, 2019, Sanofi terminated the Sanofi Collaboration Agreement. We own the material intellectual property rights developed under the sickle cell and hemophilia programs 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 December 31, 2019, in connection with the development of THR-149, and up to €16.5 million in regulatory milestone payments (e.g., €5 million for granting of first regulatory approval in either the US 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, 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 four patent families directed to novel scaffolds, and 16 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 69 patent families directed to the composition of matter of bicyclic peptides and related conjugates, and seven 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 December 31, 2019, our patent portfolio included four patent families directed to novel scaffolds, 16 patent families directed to our platform technology, 69 patent families directed to bicyclic peptides and related conjugates, and seven patent families directed to clinical indications and other properties of development assets. In total, as of December 31, 2019, we owned 90 patents in the U.S. and in Australia, Canada, China, Europe, Hong Kong, Japan, New Zealand, Russia and Singapore, with terms expiring at various dates in February 2029 to November 2037 exclusive of potential patent term adjustment and/or patent term extension.

In addition, as of December 31, 2019, we had 162 patent applications pending in the U.S. and in Argentina, Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Korea, New Zealand, Russia, Singapore, Taiwan, and Venezuela, as well as pending international applications under the Patent Cooperation Treaty (PCT), 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 December 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, there are a variety of regulations in other jurisdictions governing, among other things, clinical trials, commercial sales and distribution of medicinal products. Even if FDA approval of a particular product is obtained, 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. Currently in the European Union, for example, a clinical trial application must be submitted to each country's national regulatory authority in which the clinical trial is to take place, together with an independent ethics committee, much like the FDA and IRB, respectively. It is expected, however, that the Clinical Trials Regulation 536/2014 shall start to apply during the course of 2020. This new Regulation takes direct effect in each European Union Member State and seeks to simplify and streamline the approval of clinical trials in the European Union, for example, by allowing the clinical trial sponsor to submit a single application for approval of a

clinical trial across the EU via a new EU Portal. The new Regulation also aims to streamline and simplify the rules on safety reporting and introduces enhanced transparency requirements, such as mandatory submission of a summary of the clinical trial results to a new EU Database.

Medicinal products can only be commercialized in the European Economic Area after a marketing authorization, or MA, has been obtained. There are two types of marketing authorizations:

- The centralized 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 entirety 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 an active substance not authorized in the EEA before May 20, 2004, for products that constitute a significant therapeutic, scientific or technical innovation or for which a centralized authorization would be in the interest of patients.

- 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.

The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic or biosimilar application. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. Products receiving orphan designation, can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product's market exclusivity 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. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;

- the applicant consents to a second orphan medicinal product application; or

- the applicant cannot supply sufficient quantities of the orphan medicinal product.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention

or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and scientific assistance for study proposals. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

In the European Union, companies developing a new medicinal product must agree to a Paediatric Investigation Plan, or PIP, with the EMA and must conduct pediatric clinical trials in accordance with that PIP, unless a deferral or waiver applies, (e.g., because the relevant disease or condition occurs only in adults). The MA application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted. For other countries outside of the European Union, such as certain 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.

Additionally, we may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics.

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, as defined by such law, 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, as well as ownership and investment interests held by, during the previous year,

physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives.

In addition, we may be subject to certain analogous state and foreign laws of each of the above federal healthcare laws. In some instances, such laws may be broader in scope than its federal counterpart, such as certain state anti-kickback and false claims laws, which may apply to claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers. In addition, certain states and local jurisdictions 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 and other healthcare professionals. Additionally, we may be subject to state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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, significant administrative, civil and criminal penalties, damages, fines, disgorgement, imprisonment, 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 now provide a 70% 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.

There remain judicial and Congressional challenges to certain aspects of the ACA, as well as 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, eliminating 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. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

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 2029 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. At the federal level, the Trump administration's budget proposal for fiscal year 2020 contained further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. 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 May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January

1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Although a number of these, and other measures may require authorization 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.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit, and the United Kingdom officially withdrew from the European Union on January 31, 2020. The United Kingdom and the European Union are currently in a transition period during which the United Kingdom and the European Union are negotiating additional arrangements, including their future trading arrangement. The United Kingdom has stated that it wants the transition period to expire, and the future trading terms to be agreed, by December 31, 2020.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, immediately following Brexit, it is expected that the United Kingdom's regulatory regime will remain aligned with EU regulations. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom. In the longer term, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom.

Employees

As of December 31, 2019, we had 72 full-time or part-time employees, including 31 with M.D. or Ph.D. degrees. Of these employees, 58 employees are engaged in research and development activities and 14 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.

Corporate Information

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 our IPO, was re-registered as a public limited company named Bicycle Therapeutics plc. Bicycle Therapeutics plc is 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, 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.

Available Information

Our website address is http://www.bicycletherapeutics.com. We make available on our website, free of charge, our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov. The information

found on our website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC.

Item 1A Risk Factors.

Investing in our American Depositary Shares, or ADSs, involves a high degree of risk. The following information about these risks, together with the other information appearing elsewhere in this Annual Report on Form 10-K, including our consolidated financial statements and related notes thereto, should be carefully considered before a decision to invest in our ADSs. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. Additional risks that are currently unknown to us or that we currently believe to be immaterial may also impair our business. In these circumstances, the market price of our ADSs could decline and holders of our ADSs may lose all or part of their investment. We cannot provide assurance that any of the events discussed below will not occur.

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. Since inception, we have incurred recurring losses, including losses of $30.6 million, $21.8 million and $16.3 million for the years ended December 31, 2019, 2018 and 2017, respectively. In addition, our accumulated deficit as of December 31, 2019 was $100.6 million. 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' equity (deficit) 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, tumor-targeted immune cell agonist programs, and our other pipeline programs;
- 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. (acquired by Sanofi), or Bioverativ, Oxurion NV (formerly ThromboGenics NV), or Oxurion, and Dementia Discovery Fund, or DDF. 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 holders of our ADSs or ordinary shares 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, any current or prospective holder of our ADSs or ordinary shares 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 made 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 and reliance should not be made upon the results of any quarterly or annual periods as indications of future operating performance.

We may 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, 2019, 2018 and 2017, we used $28.6 million, $26.1 million, and $1.4 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, 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 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, 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 our existing cash of $92.1 million as of December 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of filing of this Annual Report on Form 10-K. 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 or holders of our ADSs, 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, the ownership interest of existing holders of our ADSs or ordinary shares will be diluted and the terms may include liquidation or other preferences that adversely affect existing holders' rights. 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 and tumor-targeted immune cell agonist programs 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 and tumor-targeted immune cell agonist programs.

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. In addition, we are evaluating BT5528, our first second-generation BTC that targets EphA2 and carries a monomethyl auristatin E, or MMAE cytotoxin payload, in an ongoing, company-sponsored Phase I/II clinical trial to assess safety, tolerability and efficacy in patients with solid tumors. We are also developing BT8009, targeting Nectin-4, and BT7480, which is a tumor-targeted immune cell agonist targeting Nectin-4 and agonizing CD137, for oncology indications. These target proteins have an established role in cell invasion and metastasis and are overexpressed in many solid tumors. There can be no assurance our BTCs or *Bicycle* tumor-targeted immune cell agonists 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 U.S. Food and Drug Administration, or FDA, in the U.S., European Medicines Agency, or 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, tumor-targeted immune cell agonists, 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 provide assurance 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 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 United States. 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 seven 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. As of February 13, 2020, the most recent date for which information has been provided by the CRUK, the most common treatment-related adverse events (>15%, n=39) in subjects exposed to BT1718 in the ongoing Phase I/IIa clinical trial were anemia, diarrhea, nausea, vomiting, fatigue, alanine aminotransferase increase, aspartate aminotransferase increase, gamma-glutamyltransferase increase, decreased appetite, lethargy, peripheral neuropathy, and weight decrease.

If unacceptable side effect profiles 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 rarer, 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.

The withdrawal of the United Kingdom from the European Union, commonly referred to as "Brexit," may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom will be subject to a transition period until December 31, 2020, or the Transition Period, during which European Union rules will continue to apply. Negotiations between the United Kingdom and the European Union are expected to continue in relation to the customs and trading relationship between the United Kingdom and the European Union following the expiry of the Transition Period.

The potential impact on our results of operations and liquidity resulting from Brexit remains unclear. The actual effects of Brexit will depend upon many factors and significant uncertainty remains with respect to the terms of the ultimate resolution of the Brexit negotiations.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from European Union directives and regulations, Brexit, following the Transition Period, could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. For example, as a result of

the uncertainty surrounding Brexit, the EMA relocated to Amsterdam from London. Following the Transition Period, the United Kingdom will no longer be covered by the centralized procedures for obtaining European Union-wide marketing authorization from the EMA and, unless a specific agreement is entered into, a separate process for authorization of drug products, including our product candidates, will be required in the United Kingdom, the potential process for which is currently unclear. 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, BT5528, 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, 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, and prohibitions on the promotion of an approved product for uses not included in the product's approved labeling. 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 may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict manufacturer's communications on the subject of off-label use of their products.

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-specific antibodies.

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.

We or our collaborators will be required to obtain coverage and reimbursement for companion diagnostic tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. There is significant uncertainty regarding our and our collaborators ability to obtain coverage and adequate reimbursement for any companion diagnostic test for the same reasons applicable to 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, including the FCA, and civil monetary penalty laws, 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, as well as ownership and investment interests held, during the previous year 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 FCA, 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 significant 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 share 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, significant administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, imprisonment, 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 may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any

product candidates for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products, (iv) restriction on coverage, reimbursement, and pricing for our products, (v) transparency reporting obligations regarding transfers of value to health care professionals or (vi) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect our business, financial condition and results of operations.

Among policy makers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Affordable Care Act, or ACA, was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, created 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, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D.

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. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost- sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The case was appealed to the U.S. Supreme Court, which heard oral arguments in December 2019, but has not yet issued a ruling. The full effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

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, several bills affecting implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or the Tax Act, includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act 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.” In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the ACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” In December 2018, CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to

determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, 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.

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. At the federal level, the Trump administration's budget proposal for fiscal year 2020 contained further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, 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. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and, at the same, has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative, administrative and executive measures, including the President's issuance of future executive orders, to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or 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 1 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 pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation, administrative or executive action. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated

revenue 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.

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, our employees and our 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 the 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, natural disasters, including earthquakes, typhoons, floods and fires, or public health crises, including outbreaks of novel coronavirus or H1N1 flu.

Any or all of these factors could have a material adverse impact on our business, financial condition and results of operations.

The novel coronavirus outbreak could impact our business.

In December 2019, a novel strain of coronavirus was reported in China. This virus has now spread to numerous other countries, including the United Kingdom and the United States. While we do not currently have significant operations in geographical locations where the coronavirus was initially reported to be most prevalent, we source certain research and development, consulting and other services and supplies from vendors in Asia and in Italy, where the coronavirus has become increasingly prevalent. We cannot reasonably estimate at this time the impact, if any, that the coronavirus may have on our business or operations. The extent to which the coronavirus impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact including on financial markets or otherwise.

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 governed by the provisions of the General Data Protection Regulation, or the GDPR, which became effective and enforceable across all then-current member states of the European Union on May 25, 2018. In the United Kingdom, the Data Protection Act 2018 complements the GDPR. Following the United Kingdom's withdrawal from the European Union on January 31, 2020, pursuant to the transitional arrangements agreed between the United Kingdom and European Union, the GDPR will continue to have effect in United Kingdom law until December 31, 2020 in the same fashion as was the case prior to that withdrawal as if the United Kingdom remained a member state of the European Union for such purposes. Following December 31, 2020, it is likely that the data protection obligations of the GDPR will continue to apply to United Kingdom-based organization's processing of personal data in substantially unvaried form and fashion, for at least the

short term thereafter. The GDPR enhances data protection obligations for both processors and controllers of personal data, including by materially expanding the definition of what is expressly noted to constitute personal data, requiring additional disclosures about how personal data is to be used, imposing limitations on retention of personal data, creating mandatory data breach notification requirements in certain circumstances, and establishing onerous new obligations on services providers who process personal data simply on behalf of others, as well as obligations regarding the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Economic Area to third countries (including the United States). The GDPR has expanded its reach to include any business, regardless of its location, that processes personal data in relation to the offering of goods or services to individuals in the European Union and/or the monitoring of their behavior. This expansion would incorporate any potential clinical trial activities in European Union member states. The GDPR imposes special protections for "sensitive information" which includes health and genetic information of data subjects residing in the European Union. The 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. Failure to comply with the requirements of the GDPR may result in fines of up to 4% of an undertaking's total global annual turnover for the preceding financial year, or € 20,000,000, whichever is greater. In addition to administrative fines, a wide variety of other potential enforcement powers are available to competent authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. While we have taken steps to comply with the GDPR, and implementing legislation in applicable member states, including by seeking to establish appropriate lawful bases for the various processing activities we carry out as a controller, reviewing our security procedures, and entering into data processing agreements with relevant customers and business partners, we cannot assure you that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful.

Legal, political and economic uncertainty surrounding the exit of the United Kingdom from the European Union may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the United Kingdom and pose additional risks to our business, revenue, financial condition, and results of operations.

Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union following the United Kingdom's withdrawal from the European Union on January 31, 2020, the United Kingdom will be subject to a Transition Period during which EU rules will continue to apply. Negotiations between the United Kingdom and the European Union are expected to continue in relation to the customs and trading relationship between the United Kingdom and the European Union following the expiry of the Transition Period.

The lack of clarity over which EU laws and regulations will continue to be implemented in the United Kingdom after the Transition Period (including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws) may negatively impact foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict access to capital.

The uncertainty concerning the United Kingdom's legal, political and economic relationship with the European Union after the Transition Period may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise).

These developments, or the perception that any of them could occur, 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 limit 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 United Kingdom's financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

If the United Kingdom and the European Union are unable to negotiate acceptable trading and customs terms or if other EU Member States pursue withdrawal, barrier-free access between the United Kingdom and other EU Member States or among the European Economic Area, or EEA, overall could be diminished or eliminated. The long-term effects of Brexit will depend on any agreements (or lack thereof) between the United Kingdom and the European Union and, in particular, any arrangements for the United Kingdom to retain access to EU markets after the Transition Period.

Such a withdrawal from the European Union is unprecedented, and it is unclear how the United Kingdom's access to the European single market for goods, capital, services and labor within the European Union, or single market, and the wider commercial, legal and regulatory environment, will impact our U.K. operations and customers. Our U.K. operations service customers in the United Kingdom as well as in other countries in the European Economic Area, or EEA, and these operations could be disrupted by Brexit, particularly if there is a change in the United Kingdom's relationship to the single market.

There may continue to be economic uncertainty surrounding the consequences of Brexit which could adversely impact customer confidence resulting in customers reducing their spending budgets on our solutions, which could adversely affect our business, revenue, financial condition, results of operations and could adversely affect the market price of our ADSs.

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 and Asia that are billed in U.S. dollars. 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, Oxurion, and DDF, 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, and will sponsor and fund a Phase I/IIa study for BT7401. 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 provide assurance 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., and its affiliates, or Pepscan, related to a non-exclusive patent license agreement that our subsidiary, BicycleRD Limited, or BicycleRD, entered into with Pepscan in 2009. Pursuant to the patent license agreement, BicycleRD licensed rights related to the scaffold used for *Bicycles* contained in certain of our product candidates, including our lead product candidate, BT1718, which is currently in clinical trial sponsored by CRUK, and in THR-149, which has been licensed to Oxurion. The agreement required BicycleRD to enter into a framework services agreement with Pepscan under which Pepscan would provide certain *Bicycles* not produced by BicycleRD. In 2010, BicycleRD entered into such a framework services agreement. In 2015, BicycleRD terminated the framework services agreement in accordance with its terms. Since 2015, we have ceased using the scaffolds claimed by Pepscan in our new product candidates and have instead developed proprietary scaffold technology of our own.

In 2016, Pepscan terminated the patent license agreement. BicycleRD instituted proceedings in the District Court of The Hague, or the District Court, to contest the right of Pepscan to terminate the patent license agreement. BicycleRD included a conditional claim for a ruling that the licensed patent relevant to BicycleRD's activities is invalid. In response, Pepscan claimed, among other things, that the termination of the framework services agreement and alleged breaches by BicycleRD of confidentiality obligations constituted grounds for the termination of the patent license agreement. In an interlocutory judgement delivered in April 2018, the District Court 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 reserved for further proceedings a decision on both the validity of the Pepscan patent and the question of whether BicycleRD breached its confidentiality obligations.

In July 2018, Pepscan appealed the decision of the District Court and the proceedings before the District Court were stayed pending a decision in that appeal.

On February 18, 2020, the Court of Appeal of The Hague, or the Court of Appeal, ruled that Pepscan was entitled to terminate the license agreement and granted a worldwide injunction against BicycleRD exploiting the licensed Pepscan patents and any related know-how, subject to a civil daily fine of EUR 25,000 in the event of non-compliance. BicycleRD intends to appeal the decision of the Court of Appeal to the Dutch Supreme Court and is preparing for further proceedings before the District Court, in particular concerning BicycleRD's invalidity claim, the claim related to know-how and the assessment of damages should a proceeding for such an assessment be initiated by Pepscan.

There can be no assurance that BicycleRD will prevail in any future proceedings. While we do not believe the injunction applies to entities other than BicycleRD, including our collaboration partners, there can be no assurance that Pepscan will not allege that the injunction applies to other entities.

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 December 31, 2019, 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.

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 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 are being or may be conducted, we do 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 the ability to obtain a license to obtain access to use and reference the data, including for our own regulatory submissions, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do 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 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 December 31, 2019, our intellectual property portfolio includes four patent families directed to novel scaffolds, 16 patent families directed to our platform technology, 69 patent families directed to bicyclic peptides and related conjugates, and seven 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 December 31, 2019, 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.

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 provide assurance 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, BicycleRD is involved in ongoing litigation with Pepscan in relation to a patent license agreement, pursuant to which BicycleRD licensed rights related to the scaffold used for *Bicycles* contained in our lead product candidate, BT1718, which is currently in clinical trial sponsored by CRUK, and in THR-149, which has been licensed to Oxurion. 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 BicycleRD had breached certain confidentiality obligations, which was alleged to constitute sufficient grounds for the termination of its 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 December 31, 2019, we had 72 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 provide assurance 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. We have been the target of cyber-attacks in the past. For example, we were recently targeted in a phishing incident, which included email accounts being accessed by unauthorized third parties. Promptly after discovery, we performed third-party investigations and as there was no evidence of access or acquisition of any personal information as a result of the incident, we believe that no further action was required under U.K, E.U. (GDPR) or U.S. federal or state law. There was no material impact to our business or financial condition. While we believe we responded appropriately, including implementing remedial measures to stop the cyber-attacks 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. We are aware that some public companies have recently received Civil Investigative Demands from the Federal Trade Commission, or FTC, requesting information and documents following disclosures of privacy or security incidents in SEC filings. The FTC has taken the position that inadequately disclosing privacy and security incidents in SEC filings may be a deceptive business practice, and the FTC has relied on SEC filings as a launching pad for incident investigations even where the filings were not inadequate. We cannot be certain that the FTC will consider our disclosure adequate or that the FTC will not rely on our disclosure to initiate an incident investigation.

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 May 2019, we adopted 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 significant 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, imprisonment, 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 office and laboratory space in Cambridge, U.K. and 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 Ownership of Our Securities

The market price of our ADSs is highly volatile, and holders of our ADSs may not be able to resell their ADSs at or above the price at which they purchased their ADSs.

The market price of our ADSs is highly volatile. Since our initial public offering, or IPO, in May 2019, through March 5, 2020, the trading price of our ADSs has ranged from $17.99 to $6.24. 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, holders of our ADSs may not be able to sell their ADSs at or above price at which they purchased their ADSs. 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;
- changes in the structure of healthcare payment systems;
- 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.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

An active trading market for our ADSs may not be sustained.

Prior to our IPO in May 2019, there had been no public market for our ADSs. Although our ADSs are listed on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our ADSs is not sustained, it may be difficult for holders of our ADSs to sell ADSs without depressing the market price for the shares, or at all.

An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling additional shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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 depends 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. Although we have obtained research coverage from certain analysts, there can be no assurance that analysts will continue to cover us or provide favorable 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.

As of December 31, 2019, our executive officers, directors, greater than 5% shareholders and their affiliates beneficially own approximately 78.6% of our ordinary shares and ordinary shares in the form of ADSs. Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group could 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 holders of our ADSs may believe are in their best interest as holders of our ordinary shares or ADSs. Some of these persons or entities may have interests different than current holders of our ordinary shares and ADSs. For example, because many of these shareholders purchased their ordinary shares at prices substantially below the current trading price of our ADSs 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 our ADSs 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 current trading prices of the ADSs. 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, holders of an aggregate of approximately 11,152,664 ordinary shares 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. We have also registered our ordinary shares that we may issue under our equity compensation plans. These ordinary shares may be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We have broad discretion in the use of our cash reserves and may not use them effectively.

Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our ordinary shares or ADSs. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our ADSs to decline, and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our ADSs in the foreseeable future, capital appreciation, if any, will be the sole source of gains for holders of our ADSs, and they may never receive a return on their 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 a holder's sole source of gains for the foreseeable future, and holders will suffer a loss on their investment if they are unable to sell their ADSs at or above the original purchase price.

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 2024, (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;
- 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 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 with ADSs that 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.

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.

We are 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.

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, indirectly or constructively through the application of attribution rules) 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 2019 taxable year and we do not expect to be a CFC in the 2020 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) 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. 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:

- an individual who is a citizen or individual resident of the United States;
- 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;

- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

- 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.

If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. holders.

Under the Code, we will be a passive foreign investment company, or 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 not a PFIC in the 2019 taxable year. 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. As a result, there can be no assurance regarding if we will be PFIC or will not be a PFIC in the future. In addition, 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 and our corporate structure.

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 an entity incorporated and tax resident in the United Kingdom, 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. 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 losses 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 carry them 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. An update on the proposal and the timing of its introduction is expected from the U.K. government on or after March 11, 2020 as part of the U.K. annual 'budget' fiscal event.

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, while we believe that we operate in compliance with applicable transfer pricing laws and intend to continue to do so, our transfer pricing procedures are not binding on applicable tax authorities. 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.

Provisions in the U.K. City Code on Takeovers and Mergers that may have anti-takeover effects do not apply to us.

The U.K. City Code on Takeovers and Mergers, or the Takeover Code, applies to an offer for, among other things, a public company whose registered office is in the United Kingdom if the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom (or the Channel Islands or the Isle of Man). This is known as the "residency test." The test for central management and control under the Takeover Code is different from that used by the U.K. tax authorities. Under the Takeover Code, the Takeover Panel will determine whether we have our place of central management and control in the United Kingdom by looking at various factors, primarily where the directors are resident.

In September 2019, the Takeover Panel Executive confirmed that, based on our current circumstances, we are not subject to the Takeover Code. As a result, our shareholders are not entitled to the benefit of certain takeover offer protections provided under the Takeover Code. We believe that this position is unlikely to change at any time in the near future but, in accordance with good practice, we will review the situation on a regular basis and consult with the

Takeover Panel if there is any change in our circumstances which may have a bearing on whether the Takeover Panel would determine our place of central management and control to be in the United Kingdom.

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 2006, 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. 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. 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, if we were 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, as well as the sanction of the U.K. court;
- 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 that 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

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.

ITEM 3. LEGAL PROCEEDINGS.

From time to time, we may become subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Other than as described below, we are not currently subject to any material legal proceedings.

License Litigation

In 2009, our subsidiary, BicycleRD Limited, or BicycleRD, entered into a non-exclusive patent license agreement with Pepscan Systems B.V. and its affiliates, or Pepscan, pursuant to which it licensed rights related to the scaffold used for *Bicycles* contained in our lead product candidate, BT1718, which is currently in clinical trial sponsored by CRUK, and in THR-149, which has been licensed to Oxurion. The agreement required BicycleRD to enter into a framework services agreement with Pepscan under which Pepscan would provide certain *Bicycles* not produced by BicycleRD. In 2010, BicycleRD entered into such a framework services agreement. In 2015, BicycleRD terminated the framework services agreement in accordance with its terms. In 2016, Pepscan terminated the patent license agreement. Since 2015, we have ceased using the scaffolds claimed by Pepscan in our new product candidates and have instead developed proprietary scaffold technology of our own.

BicycleRD instituted proceedings in the District Court of The Hague, or the District Court, to contest the right of Pepscan to terminate the patent license agreement. BicycleRD included a conditional claim for a ruling that the licensed patent relevant to BicycleRD's activities is invalid. In response, Pepscan claimed, among other things, that the termination of the framework services agreement and alleged breaches by BicycleRD of confidentiality obligations constituted grounds for the termination of the patent license agreement.

In a interlocutory judgement delivered in April 2018, the District Court 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 reserved for further proceedings a decision on both the validity of the Pepscan patent and the question of whether BicycleRD breached its confidentiality obligations. In July 2018, Pepscan appealed the decision of the District Court and the proceedings before the District Court were stayed pending a decision in that appeal.

On February 18, 2020, the Court of Appeal of The Hague, or the Court of Appeal, ruled that Pepscan was entitled to terminate the license agreement and granted a worldwide injunction against BicycleRD exploiting the licensed Pepscan patents and any related know-how, subject to a civil daily fine of EUR 25,000 in the event of non-compliance. BicycleRD intends to appeal the decision of the Court of Appeal to the Dutch Supreme Court and is preparing for further proceedings before the District Court, in particular concerning BicycleRD's invalidity claim, the claim related to know-how and the assessment of damages should a proceeding for such an assessment be initiated by Pepscan.

Pending such further proceedings, BicycleRD will comply with the injunction issued by the Court of Appeal. The injunction by its terms applies only to BicycleRD.

The patent that is the subject of these proceedings expires in February 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 Annual Report on Form 10-K, 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 filing date of this Annual Report on Form 10-K, no decision has been issued by the European Patent Office in respect of these appeals.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Market Information

Our ordinary shares, par value £0.01 per share, are not publicly traded. Our American Depositary Shares, or ADSs, each represent one ordinary share of Bicycle Therapeutics plc and began trading on The Nasdaq Global Select Market on May 23, 2019 under the symbol "BCYC." Prior to that date, there was no public trading market for our ADSs or our ordinary shares.

Holders of Ordinary Shares

As of March 5, 2020, there were approximately 75 holders of record of our ordinary shares and one holder of record of our ADSs. The number of beneficial owners of the ADSs in the United States is likely to be much larger than the number of record holders of our ordinary shares in the United States.

Recent Sales of Unregistered Equity Securities

None.

Use of Proceeds from Registered Securities

On May 28, 2019, we completed our IPO of 4,333,333 ADSs at a public offering price of $14.00 per ADS for an aggregate offering price of approximately $60.7 million. In addition, in June 2019, we issued 304,333 ADSs at a public offering price of $14.00 per ADS for an aggregate offering price of approximately $4.3 million in connection with the underwriters' partial exercise of their option to purchase additional ADSs. Goldman Sachs & Co. LLC, Jefferies LLC, Piper Jaffray & Co. and Canaccord Genuity LLC served as the underwriters of the IPO. The offer and sale of all of the ADSs in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-231076), which was declared effective by the SEC on May 22, 2019.

We received aggregate net proceeds from the offering of approximately $56.4 million, after deducting underwriting discounts and commissions of $4.5 million and offering expenses of $4.0 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates.

There has been no material change in our planned use of the net proceeds from the offering as described in the final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act. As of December 31, 2019, we consumed approximately $15.8 million of the net proceeds from the IPO, primarily to advance our BT1718, BT5528, BT8009, BT7480, and other discovery development programs, as well as for continued drug discovery efforts and translational research activities, and for working capital and other general corporate purposes. We have invested the remaining net proceeds from our IPO in interest bearing cash accounts.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. SELECTED FINANCIAL DATA.

You should read the following selected financial data together with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the accompanying notes included elsewhere in this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2019, 2018 and 2017 and the balance sheet data as of December 31, 2019 and 2018 from our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. We have derived the balance sheet data as of December 31, 2017 from our audited consolidated financial statements not included in this report. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year ended December 31,		
	2019	2018	2017
	(in thousands, except share and per share data)		
Statement of Operations Data:			
Collaboration revenues	$ 13,801	$ 7,136	$ 2,060
Operating expenses:			
Research and development	25,540	20,761	11,866
General and administrative	14,560	8,121	6,407
Total operating expenses	40,100	28,882	18,273
Loss from operations	(26,299)	(21,746)	(16,213)
Other income (expense):			
Interest and other income	814	169	50
Other expense, net	(5,377)	(665)	(119)
Total other expense, net	(4,563)	(496)	(69)
Net loss before income tax provision	(30,862)	(22,242)	(16,282)
Benefit from income taxes	(254)	(396)	(23)
Net loss	$ (30,608)	$ (21,846)	$ (16,259)
Net loss attributable to ordinary shareholders	$ (30,608)	$ (21,846)	$ (16,259)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (2.77)	$ (49.78)	$ (48.81)
Weighted average ordinary shares outstanding, basic and diluted	11,045,370	438,862	333,125

See Note 2 within the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to calculated basic and diluted net loss per share applicable to ordinary shareholders.

	As of December 31,		
	2019	2018	2017
	(in thousands)		
Balance Sheet Data:			
Cash	$ 92,117	$ 63,380	$ 67,663
Working capital	95,325	67,840	62,061
Total assets	110,194	81,626	74,001
Total deferred revenue	5,657	14,635	14,467
Warrant liability	—	4,804	4,411
Convertible preferred shares	—	122,197	96,441
Total shareholders' equity (deficit)	$ 93,198	$ (69,826)	$ (47,184)

ITEM 7. 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 Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, 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 Annual Report on Form 10-K, 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 "Forward-Looking Statements."

For the discussion of the financial condition and results of operations for the year ended December 31, 2018 compared to the year ended December 31, 2017, refer to "Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations" and "—Liquidity and Capital Resources" included in the final prospectus forming a part of the registration statement declared effective by the SEC in connection with our initial public offering, or IPO, and filed pursuant to Rule 424(b) under the Securities Act on May 23, 2019.

Overview

We are a clinical-stage biopharmaceutical company developing a novel and differentiated 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, making *Bicycles* attractive candidates for drug development. *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. The relatively large surface area presented by *Bicycles* allow targets to be drugged that have historically been intractable to non-biological approaches. *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 are also evaluating BT5528, a second-generation BTC targeting Ephrin type-A receptor 2, or EphA2, in a Company-sponsored Phase I/II study and conducting Investigational New Drug application, or IND, -enabling activities for BT8009, a BTC targeting Nectin-4. Our discovery pipeline in oncology includes *Bicycle*-based systemic immune cell agonists and *Bicycle* tumor-targeted immune cell agonists (TICAs™).

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, 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, BT8009, BT7480 and BT7401, 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 ADSs and ordinary shares, 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 Sanofi. Since our inception in 2009 through December 31, 2019, we have received gross proceeds of $193.1 million from the sale of ADSs, ordinary shares and convertible preferred shares, including the proceeds from our initial public offering, and $30.2 million of cash payments under our collaboration revenue arrangements, including $4.1 million from Oxurion, $9.0 million from AstraZeneca, $15.0 million from Sanofi and $1.1 million from DDF. 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 $30.6 million, $21.8 million and $16.3 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $100.6 million. 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 continue to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses. 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 and BT5528;
- progress the preclinical and clinical development of BT8009, BT7480 and BT7401;
- 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 operations as a public company.

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 December 31, 2019, we had cash of $92.1 million. We believe that our existing cash will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of filing of this Annual Report on Form 10-K. 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.”

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, Sanofi, Oxurion, and DDF, 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, Cancer Research Technology Limited may elect to receive 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 in 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 and BT5528; (ii) initiate clinical trials for our product candidates, including BT8009 and BT7480 and BT7401; 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 and BT5528;
- progressing the preclinical and clinical development of BT8009, BT7480 and BT7401;
- 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

Prior to our IPO, other expense, net consisted 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 remeasured the warrant liability at fair value at each reporting period until completion of our IPO in May 2019. Upon the completion of the IPO, the respective warrants were exercised or converted to warrants to subscribe for ordinary shares, and as such, we will not incur additional expense related to the remeasurement of the warrant liability in future periods.

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 benefit from income taxes presented in our consolidated statements of operations and comprehensive loss represents the tax impact from our operating activities in the United States, which generates taxable income 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, 2019. 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 $41.7 million and $29.1 million as of December 31, 2019 and 2018.

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

The following table summarizes our results of operations for the years ended December 31, 2019, 2018 and 2017:

	Year Ended December 31,		
	2019	2018	2017
	(in thousands)		
Collaboration revenues	$ 13,801	$ 7,136	$ 2,060
Operating expenses:			
Research and development	25,540	20,761	11,866
General and administrative	14,560	8,121	6,407
Total operating expenses	40,100	28,882	18,273
Loss from operations	(26,299)	(21,746)	(16,213)
Other income (expense):			
Interest and other income	814	169	50
Other expense, net	(5,377)	(665)	(119)
Total other expense, net	(4,563)	(496)	(69)
Net loss before income tax provision	(30,862)	(22,242)	(16,282)
Benefit from income taxes	(254)	(396)	(23)
Net loss	$ (30,608)	$ (21,846)	$ (16,259)

Comparison of the Years Ended December 31, 2019 and 2018

	December 31,		
	2019	2018	Change
	(in thousands)		
Collaboration revenues	$ 13,801	7,136	$ 6,665
Operating expenses:			
Research and development	25,540	20,761	4,779
General and administrative	14,560	8,121	6,439
Total operating expenses	40,100	28,882	11,218
Loss from operations	(26,299)	(21,746)	(4,553)
Other income (expense):			
Interest and other income	814	169	645
Other expense	(5,377)	(665)	(4,712)
Total other expense, net	(4,563)	(496)	(4,067)
Net loss before income tax provision	(30,862)	(22,242)	(8,620)
Benefit from income taxes	(254)	(396)	142
Net loss	$ (30,608)	(21,846)	$ (8,762)

Collaboration Revenues

Collaboration revenues increased by $6.7 million during the year ended December 31, 2019 compared to the year ended December 31, 2018, primarily due to an increase of $6.7 million of revenue from our collaboration with Sanofi. In March 2019, Sanofi exercised its right to terminate the sickle cell program and in October 2019, Sanofi terminated the hemophilia program, resulting in the recognition of revenue of $5.3 million and $4.7 million, respectively, for amounts allocated to material rights when these options expired. These amounts were offset by a decrease in research services revenue, which services were substantially completed in the second quarter of 2019. Additional increases in collaboration revenue included an increase of $1.0 million of revenue under a material transfer agreement and an increase of $0.4 million of revenue from a collaboration arrangement with DDF, which was entered into in May 2019. These amounts were offset by a decrease of $1.7 million of revenue under our collaboration with Oxurion, primarily due to $1.2 million of revenue recognized for certain development milestones achieved during the year ended December 31, 2018 that did not recur in the year ended December 31, 2019.

Research and Development Expenses

The following table summarizes our research and development expenses for the years presented:

	Year Ended December 31,		
	2019	2018	Change
	(in thousands)		
BT1718 (MT1)	$ 1,211	$ 1,546	$ (335)
BT5528 (EphA2)	3,878	4,569	(691)
BT8009 (Nectin-4)	3,260	2,797	463
Tumor-targeted immune cell agonist	1,082	—	1,082
Other discovery and platform related expense	11,125	8,702	2,423
Employee and contractor related expenses	9,122	7,185	1,937
Share-based compensation	1,289	513	776
Facility expenses	1,297	1,328	(31)
Research and development incentives	(6,724)	(5,879)	(845)
Total research and development expenses	$ 25,540	$ 20,761	$ 4,779

Research and development expense increased by $4.8 million in the year ended December 31, 2019 as compared to year ended December 31, 2018, primarily due to increases of $0.5 million and $1.1 million in the BT8009 and tumor-targeted immune cell agonist program spending, respectively, $2.4 million in other unallocated discovery and platform related expense, $1.9 million in employee and contractor-related expense due to an increase in headcount as we expanded our operations in the United States and the United Kingdom and $0.8 million of share-based compensation expense. These expenses were offset by a decrease of $0.7 million in BT5528 program spending due to the timing of IND-enabling activities in 2018, as well as an increase in 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 beginning at candidate nomination and accumulate all costs incurred to support each program to date. Through December 31, 2019, we have incurred approximately $12.9 million, $8.4 million, $6.1 million and $1.1 million of direct expenses for the development of the BT1718, BT5528, BT8009 and tumor-targeted immune cell agonist programs, respectively.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years presented:

	Year Ended December 31,		
	2019	2018	Change
	(in thousands)		
Personnel related costs	$ 4,594	$ 2,946	$ 1,648
Professional and consulting fees	6,084	3,574	2,510
Other general and administration costs	2,983	1,361	1,622
Share-based compensation	1,797	554	1,243
Effect of foreign exchange rates	(898)	(314)	(584)
Total general and administrative expenses	$ 14,560	$ 8,121	$ 6,439

General and administrative expenses increased by $6.4 million for the year ended December 31, 2019 as compared to the year ended December 31, 2018, primarily due to increases of $1.6 million in personnel related costs due to an increase in headcount as we expanded our operations in the United States and the United Kingdom, $1.2 million in share-based compensation expense as a result of an increase in fair value of our ordinary shares and share options following our IPO, as well as $2.5 million in professional fees, including legal, human resources, marketing and

consulting costs and $1.6 million in other general and administrative cost, including insurance costs to support our operations as a public company. These amounts were offset by an increase of $0.6 million in gains from the effect of foreign exchange rates during year ended December 31, 2019.

Other Expense, net

Other expense, net increased by $4.1 million for the year ended December 31, 2019, as compared to the year ended December 31, 2018, primarily due to $4.7 million of additional expense associated with changes in the fair value of the warrant liability and final re-measurement upon completion of the IPO, offset by higher interest income of $0.6 million as a result of a higher cash balance due to proceeds from our IPO.

Liquidity and Capital Resources

From our inception through December 31, 2019, we have not generated any revenue from product sales and have 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 ordinary shares (including in the form of ADSs) and 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, Sanofi, and DDF.

From our inception in 2009 through December 31, 2019, we have received gross proceeds of $193.1 million from the sale of ordinary shares (including in the form of ADSs) and convertible preferred shares, including the proceeds from our IPO, as well as $30.2 million of cash payments under our collaboration revenue arrangements including $4.1 million from Oxurion, $9.0 million from AstraZeneca, $15.0 million from Sanofi, and $1.1 million from DDF.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2019, 2018 and 2017:

	Year Ended December 31,		
	2019	2018	2017
	(in thousands)		
Net cash used in operating activities	$ (28,613)	$ (26,078)	$ (1,415)
Net cash used in investing activities	(1,555)	(1,186)	(1,113)
Net cash provided by financing activities	58,440	25,430	57,876
Effect of exchange rate changes on cash	465	(2,449)	2,913
Net increase (decrease) in cash	$ 28,737	$ (4,283)	$ 58,261

Operating Activities

Net cash used in operating activities for the year ended December 31, 2019 included our net loss of $30.6 million, net cash used in our operating assets and liabilities of $7.4 million and non-cash charges of $9.4 million, which included share-based compensation expense of $3.1 million, depreciation and amortization of $1.0 million, and changes in the fair value of the warrant liability of $5.4 million. Net changes in our operating assets and liabilities for the year ended December 31, 2019, consisted primarily of a decrease in accounts receivable of $4.9 million primarily due to a payment received from AstraZeneca for its exercise of the Additional Four Target Option, a decrease in deferred revenue of $9.3 million, primarily due to the recognition of revenue related to the Sanofi collaboration arrangement, and a decrease in accrued expenses and other current liabilities of $0.9 million, an increase in prepaid expenses and other assets of $3.1 million primarily due to prepaid clinical costs, offset by an increase in accounts payable of $0.2 million and an increase in other long-term liabilities of $1.1 million.

Net cash used in operating activities for the year ended December 31, 2018 included our net loss of $21.8 million, net cash used 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 and 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 Sanofi collaboration arrangement. These amounts were offset by an increase in accrued expenses and other current liabilities of $2.6 million.

Investing Activities

During the years ended December 31, 2019 and 2018, we used $1.6 million and $1.2 million, respectively, of cash in investing activities for purchases of property and equipment consisting primarily of laboratory equipment.

Financing Activities

During the year ended December 31, 2019, net cash provided by financing activities was $58.4 million, primarily consisting of net proceeds of $57.0 million from our IPO, and net proceeds of $1.3 million from our Series B2 convertible preferred shares issued in January 2019.

During the year ended December 31, 2018, net cash provided by financing activities was $25.4 million, consisting of net proceeds of $26.0 million from the sale of our Series B2 convertible preferred shares issued in December 2018 offset by payments of $0.6 million of costs related to our IPO.

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 and BT5528;
- progress the preclinical and clinical development of BT8009, BT7480 and BT7401;
- 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 operations as a public company.

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.

As of December 31, 2019, we had cash of $92.1 million. We believe that our existing cash will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of filing of this Annual Report on Form 10-K. 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 DDF;
- 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, the ownership interests of our existing holders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing equity holders. 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, 2019 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]	$ 2,099	$ 879	$ 1,220	$ —	$ —
Total	$ 2,099	$ 879	$ 1,220	$ —	$ —

(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.

In the ordinary course of business, we enter into various agreements with contract research organizations to provide clinical trial services, 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

For a discussion of legal matters as of December 31, 2019, see Note 12 "Commitments and Contingencies," within the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K

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 elsewhere in the Annual Report on Form 10-K, 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 recognize revenue in accordance with ASU 2014-09, Revenue from Contracts with Customers (Topic 606) (“ASC 606”) and all subsequent amendments. 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. As of December 31, 2019, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-Based Compensation

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 vests 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.

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. The assumptions used in computing the fair value of stock option awards reflect our best estimates but involve uncertainties related to market and other conditions, many of which are outside of our control. Changes in any of these assumptions may materially affect the fair value of share-based awards granted and the amount of share-based compensation recognized in future periods.

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.

Research and Development Incentives and Receivable

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 our subsidiaries in the United Kingdom are reimbursed up to 14.5% of the surrenderable 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 represents an amount due in connection with the above program. We recorded a reduction to research and development expense of $6.7 million, $5.9 million and $2.9 million during the years ended December 31, 2019, 2018 and 2017, respectively.

Emerging Growth Company Status

We are an “emerging growth company,” or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, We will remain an EGC until the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of our initial public offering (December 31, 2024), (2) the last day of the fiscal year in which we have total annual gross revenue 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” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our ordinary shares held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such fiscal year or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. The JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to “opt out” of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth 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.

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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

Interest Rate Sensitivity

As of December 31, 2019, we had cash of $92.1 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 December 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 is the currency of the primary economic environment in which an entity’s operations are conducted. The functional currency of Bicycle Therapeutics plc and Bicycle Therapeutics Inc. is the United States dollar. The functional currency of 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 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 gain of $0.9 million, a foreign exchange gain of $0.3 million and a foreign exchange loss of $0.6 million for the years ended December 31, 2019, 2018 and 2017, respectively.

For financial reporting purposes, our consolidated financial statements have been translated into U.S. dollars. We translate the assets and liabilities of 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' equity (deficit) amounts are translated based on historical exchange rates as of the date of each transaction. Translation adjustments are not included in determining net loss but are included in our foreign exchange adjustment included in the consolidated statements of convertible preferred shares and shareholders' equity (deficit) 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.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

The financial statements required by this item are set forth beginning on page F-1 of this Annual Report on Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Material Weakness in Our Internal Control Over Financial Reporting

In connection with the preparation of our consolidated financial statements for the year ended December 31, 2018, we previously identified and disclosed a material weakness in our internal control over financial reporting related to the valuation of our warrant liability. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness was 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 as of 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 period ended September 30, 2018. As a result, the consolidated financial statements for those periods required restatement.

Remediation of Material Weakness

During the year ended December 31, 2019, we implemented measures designed to improve our internal control over financial reporting to remediate the identified material weakness, including by: formalizing our processes and

internal control documentation; strengthening supervisory reviews by our financial management; hiring additional qualified accounting and finance personnel to enable the implementation of internal control over financial reporting; and segregating duties amongst accounting and finance personnel. Our management has concluded, based on evidence obtained in validating the design and operating effectiveness of the controls, that the efforts undertaken to enhance the design of our controls would lead to the prevention or detection of a material misstatement of our consolidated financial statements. As such, our management concluded that we have remediated this material weakness as of December 31, 2019.

Evaluation of Disclosure Controls and Procedures.

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. Based on the evaluation of our disclosure controls and procedures as of December 31, 2019, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting.

Due to a transition period established by SEC rules applicable to newly public companies, our management is not required to evaluate the effectiveness of our internal control over financial reporting until after the filing of our Annual Report on Form 10-K for the year ended December 31, 2019.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption for "emerging growth companies."

Changes in Internal Control over Financial Reporting.

Other than described in the subsection entitled "Remediation of Material Weakness" above, there were no changes in our internal control over financial reporting that occurred during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The information required by this Item 10 will be included in the sections titled “Board of Directors and Corporate Governance” and “Information About Our Executive Officers” in our Proxy Statement and is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION.

The information required by this Item 11 will be included in the sections titled “Executive Compensation” and “Board of Directors and Corporate Governance” in our Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

The information required by this Item 12 will be included in the sections titled “Security Ownership of Certain Beneficial Owners and Management” and “Executive Compensation Plan Information” in our Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

The information required by this Item 13 will be included in the sections titled “Board of Directors and Corporate Governance” and “Transactions with Related Persons” in our Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.

The information required by this Item 14 will be included in Proposal 5 in the section titled “Independent Registered Public Account Firm Fees” in our Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

The financial statements schedules and exhibits filed as part of this Annual Report on Form 10-K are as follows:

(a)(1) Financial Statements

Reference is made to the financial statements included in Item 8 of Part II hereof.

(a)(2) Financial Statement Schedules

All other schedules are omitted because they are not required or the required information is included in the financial statements or notes thereto.

(a)(3) Exhibits

The exhibits listed below are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished:

Number	Description
3.1	Articles of Association (incorporated by reference to Exhibit 3.2 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
4.1	Form of Deposit Agreement (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
4.2	Form of American Depositary Receipt (included in Exhibit 4.1) (incorporated by reference to Exhibit 4.2 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
4.3	Registration Rights Agreement by and among Bicycle Therapeutics Limited and the Investors listed therein, dated December 21, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on April 26, 2019).
4.4	Description of Securities.
10.1+	Form of Share Option Contract of Bicycle Therapeutics Limited for employees in England (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on April 26, 2019).
10.2+	Form of Share Option Contract of Bicycle Therapeutics Limited for employees in the United States (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on April 26, 2019).
10.3+	Rules of the Bicycle Therapeutics Share Option Plan, as amended on September 12, 2019 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q (File No. 001-38916) filed with the Securities and Exchange Commission on November 7, 2019).
10.4+	Forms of award agreements under the Bicycle Therapeutics Share Option Plan, as amended.

Number	Description
10.5+	2019 Employee Share Purchase Plan (incorporated by reference to Exhibit 10.5 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
10.6+	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.4 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
10.7+	Service Agreement, dated September 26, 2019, by and between BicycleTx Ltd. and Kevin Lee (Incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K (File No. 001-38916) filed with the Securities and Exchange Commission on September 30, 2019).
10.8+	Amended and Restated Employment Agreement, dated September 26, 2019, by and between Bicycle Therapeutics Inc. and Lee Kalowski (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K (File No. 001-38916) filed with the Securities and Exchange Commission on September 30, 2019).
10.9+	Amended and Restated Employment Agreement, dated September 26, 2019, by and between BicycleTx Ltd. and Michael Skynner, Ph.D.
10.10+	Amended and Restated Employment Agreement, dated September 26, 2019, by and between Bicycle Therapeutics Inc. and Nicholas Keen, Ph.D.
10.11+	Service Agreement, dated September 26, 2019, by and between BicycleTx Ltd and Nigel Crockett.
10.12+	Form of Deed of Indemnity between the Company and each of its directors (incorporated by reference to Exhibit 10.1 to Company's Current Report on Form 8-K (File No. 001-38916), filed with the Securities and Exchange Commission on November 12, 2019).
10.13+	Form of Deed of Indemnity between the registrant and each of its executive officers (incorporated by reference to Exhibit 10.2 to Company's Current Report on Form 8-K (File No. 001-38916), filed with the Securities and Exchange Commission on November 12, 2019).
10.14+	Non-employee Director Compensation Policy.
10.15	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 (incorporated by reference to Exhibit 10.13 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
10.16	Lease Agreement, by and between Bicycle Therapeutics Inc. and King 4 Hartwell Place, LLC, dated September 26, 2017 (incorporated by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on April 26, 2019).
10.17	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 (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on April 26, 2019).

Number	Description
10.18††	Discovery Collaboration and License Agreement between BicycleTx Limited and Genentech, Inc., dated February 21, 2020.
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Company's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on April 26, 2019).
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page of this report).
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

* Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

+ Indicates a management contract or compensatory plan.

† Confidential treatment has been granted for certain portions of this exhibit. These portions have been omitted and filed separately with the SEC.

†† Portions of this Exhibit (indicated with [***]) have been omitted as the registrant has determined that (i) the omitted information is not material and (ii) the omitted information would likely cause competitive harm to the registrant if publicly disclosed.

Index to Consolidated Financial Statements of
Bicycle Therapeutics, plc

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Bicycle Therapeutics plc

Opinion on the Financial Statements

We have audited the accompanying Consolidated Balance Sheets of Bicycle Therapeutics plc and its subsidiaries (the "Company") as of December 31, 2019 and 2018, and the related Consolidated Statements of Operations and Comprehensive Loss, Consolidated Statements of Convertible Preferred Shares and Shareholders' Equity (Deficit) and Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019 in conformity with accounting principles generally accepted in the United States of America.

Change in accounting principle

As discussed in Note 2 to the consolidated financial statements, the Company has changed the manner in which it accounts for leases in 2019.

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. 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 10, 2020

We have served as the Company's or its predecessor's auditor since 2010, which includes periods before the Company become subject to SEC reporting requirements.

Bicycle Therapeutics plc

Consolidated Balance Sheets

(amounts in thousands, except share and per share data)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash	$ 92,117	$ 63,380
Accounts receivable	201	5,021
Prepaid expenses and other current assets	4,884	2,076
Research and development incentives receivable	6,944	6,292
Total current assets	104,146	76,769
Property and equipment, net	2,292	1,818
Operating lease right-of-use assets	2,056	—
Other assets	1,700	3,039
Total assets	$ 110,194	$ 81,626
Liabilities, convertible preferred shares and shareholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,949	$ 1,887
Accrued expenses and other current liabilities	6,144	7,032
Deferred revenue, current portion	728	10
Total current liabilities	8,821	8,929
Warrant liability	—	4,804
Operating lease liabilities	1,251	—
Deferred revenue, net of current portion	4,929	14,625
Other long-term liabilities	1,995	897
Total liabilities	16,996	29,255
Commitments and contingencies (Note 12)		
Series A convertible preferred shares, £0.01 nominal value; no shares and 3,000,001 shares authorized at December 31, 2019 and December 31, 2018, respectively; no shares and 2,800,001 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively	—	41,820
Series B1 convertible preferred shares, £0.01 nominal value: no shares and 4,690,485 shares authorized at December 31, 2019 and December 31, 2018, respectively; no shares and 3,947,198 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively	—	54,621
Series B2 convertible preferred shares, £0.01 nominal value: no shares and 1,403,633 shares authorized at December 31, 2019 and December 31, 2018, respectively; no shares and 1,323,248 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively	—	25,756
Shareholders' equity (deficit):		
Ordinary shares, £0.01 nominal value; 31,995,653 and 15,452,420 shares authorized at December 31, 2019 and December 31, 2018, respectively; 17,993,701 shares issued and outstanding at December 31, 2019; 898,675 shares issued and 814,728 shares outstanding at December 31, 2018	227	10
Additional paid-in capital	195,056	1,857
Accumulated other comprehensive loss	(1,535)	(1,751)
Accumulated deficit	(100,550)	(69,942)
Total shareholders' equity (deficit)	93,198	(69,826)
Total liabilities, convertible preferred shares and shareholders' equity (deficit)	$ 110,194	$ 81,626

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics plc

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2019	2018	2017
Collaboration revenues	$ 13,801	$ 7,136	$ 2,060
Operating expenses:			
Research and development	25,540	20,761	11,866
General and administrative	14,560	8,121	6,407
Total operating expenses	40,100	28,882	18,273
Loss from operations	(26,299)	(21,746)	(16,213)
Other income (expense):			
Interest and other income	814	169	50
Other expense, net	(5,377)	(665)	(119)
Total other expense, net	(4,563)	(496)	(69)
Net loss before income tax provision	(30,862)	(22,242)	(16,282)
Benefit from income taxes	(254)	(396)	(23)
Net loss	$ (30,608)	$ (21,846)	$ (16,259)
Net loss attributable to ordinary shareholders	$ (30,608)	$ (21,846)	$ (16,259)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (2.77)	$ (49.78)	$ (48.81)
Weighted average ordinary shares outstanding, basic and diluted	11,045,370	438,862	333,125
Comprehensives Loss:			
Net loss	$ (30,608)	$ (21,846)	$ (16,259)
Other comprehensive income (loss):			
Foreign currency translation adjustment	216	(1,820)	2,355
Total comprehensive loss	$ (30,392)	$ (23,666)	$ (13,904)

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics plc

Consolidated Statements of Convertible Preferred Shares and Shareholders' Equity (Deficit)

(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' Equity (Deficit)
	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	—	—	3,947,198	54,621	—	—	—	—	—	—	—	—
Issuance of restricted share awards	—	—	—	—	—	—	48,480	1	114	—	—	115
Issuance of ordinary shares upon exercise of share options	—	—	—	—	—	—	4,300	—	—	—	—	—
Share-based compensation expense	—	—	—	—	—	—	—	—	401	—	—	401
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	2,355	—	2,355
Net loss	—	—	—	—	—	—	—	—	—	—	(16,259)	(16,259)
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 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)
Issuance of convertible preferred shares	—	—	—	—	80,385	1,583	—	—	—	—	—	—
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	146	123,634	—	—	123,780
Reclassification of warrant liability to additional paid-in capital and exercise of warrants	—	—	—	—	—	—	723,992	9	10,018	—	—	10,027
Issuance of ADSs in initial public offering, net of underwriting discounts, commissions and offering expenses of $8.5 million	—	—	—	—	—	—	4,637,666	59	56,322	—	—	56,381
Issuance of restricted share awards	—	—	—	—	—	—	83,947	2	395	—	—	397
Issuance of ordinary shares upon exercise of share options	—	—	—	—	—	—	85,839	1	142	—	—	143
Share-based compensation expense	—	—	—	—	—	—	—	—	2,688	—	—	2,688
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	216	—	216
Net loss	—	—	—	—	—	—	—	—	—	—	(30,608)	(30,608)
Balance at December 31, 2019	—	$ —	—	$ —	—	$ —	17,993,701	$ 227	$ 195,056	$ (1,535)	$ (100,550)	$ 93,198

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics plc
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2019	2018	2017
Cash flows from operating activities:			
Net loss	$ (30,608)	$ (21,846)	$ (16,259)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	3,083	1,023	515
Depreciation and amortization	960	712	332
Change in fair value of warrant liability	5,381	665	119
Changes in operating assets and liabilities:			
Accounts receivable	4,909	(400)	—
Non-cash research and development expense	—	—	856
Research and development incentives receivable	(383)	(3,586)	(1,407)
Prepaid expenses and other current assets	(2,723)	(1,329)	(330)
Operating lease right-of-use assets	712	—	—
Other assets	(397)	(301)	(1,039)
Accounts payable	220	(169)	67
Accrued expenses and other current liabilities	(852)	2,557	1,267
Lease liabilities	(709)	—	—
Deferred revenue	(9,295)	(3,947)	14,081
Other long-term liabilities	1,089	543	383
Net cash used in operating activities	(28,613)	(26,078)	(1,415)
Cash used in investing activities:			
Purchases of property and equipment	(1,555)	(1,186)	(1,113)
Net cash used in investing activities	(1,555)	(1,186)	(1,113)
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	1,334	26,005	—
Proceeds from issuance of ADSs in initial public offering, net of issuance costs	56,957	(576)	—
Proceeds from the exercise of share options and sale of ordinary shares	143	1	1
Proceeds from the exercise of warrants	6	—	—
Net cash provided by financing activities	58,440	25,430	57,876
Effect of exchange rate changes on cash	465	(2,449)	2,913
Net increase (decrease) in cash	28,737	(4,283)	58,261
Cash at beginning of period	63,380	67,663	9,402
Cash at end of period	$ 92,117	$ 63,380	$ 67,663
Supplemental disclosure of cash flow information			
Cash paid for income taxes	$ 117	$ 73	$ —
Cash paid for amounts included in the measurement of operating lease liabilities	$ 891	$ —	$ —
Purchases of property and equipment included in accounts payable and accrued expenses	$ 76	$ —	$ —
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	$ —
Conversion of convertible preferred shares to ordinary shares upon closing of the initial public offering	$ 123,780	$ —	$ —
Reclassification of warrant liability to additional paid-in capital	$ 10,021	$ —	$ —

The accompanying notes are an integral part of the consolidated financial statements

Bicycle Therapeutics plc

Notes to Consolidated Financial Statements

1. Nature of the business and basis of presentation

Bicycle Therapeutics plc (collectively with its subsidiaries, the "Company") is a clinical-stage biopharmaceutical company developing a novel and differentiated 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 evaluating BT5528, a second-generation BTC targeting Ephrin type-A receptor 2, or EphA2, in a Company-sponsored Phase I/II study and conducting Investigational New Drug application, or IND, -enabling activities for BT8009, a BTC targeting Nectin-4. The Company's discovery pipeline in oncology includes *Bicycle*-based systemic immune cell agonists and *Bicycle* tumor-targeted immune cell agonists (TICAs™). Beyond oncology, the Company is collaborating with biopharmaceutical companies and organizations in therapeutic areas that include anti-infective, cardiovascular, ophthalmology and respiratory indications.

The accompanying consolidated financial statements include the accounts of Bicycle Therapeutics plc 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").

Share capital reorganization

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 initial public offering ("IPO") has been adjusted accordingly, as well as the number of ordinary shares over which options have been granted.

On May 22, 2019, Bicycle Therapeutics Limited ("BTL") re-registered as a public limited company, and changed its name to Bicycle Therapeutics plc. The Company historically conducted its business through BTL and its wholly owned subsidiaries, BicycleTx Limited, BicycleRD Limited and Bicycle Therapeutics Inc., and, therefore the historical consolidated financial statements previously presented the consolidated results of operations of BTL. Following the completion of the Company's re-registration in May 2019, the consolidated financial statements of BTL became the historical consolidated financial statements of the Company.

Initial public offering

On May 28, 2019, the Company completed its IPO, pursuant to which it issued and sold 4,333,333 American Depositary Shares ("ADSs"), representing the same number of ordinary shares at a public offering price of $14.00 per ADS. In addition, in June 2019, the Company issued and sold an additional 304,333 ADSs, pursuant to the partial

exercise of the underwriters' option to purchase additional ADSs. The aggregate net proceeds received by the Company from the IPO were $56.4 million, after deducting underwriting discounts and commissions of $4.5 million and offering expenses of $4.0 million. Upon the closing of the IPO, all of the Company's outstanding convertible preferred shares automatically converted into 11,647,529 ordinary shares, on a 1:1.429 basis. In addition, warrants to subscribe for Series A and Series B1 convertible preferred shares that were not exercised in conjunction with the IPO automatically became warrants to subscribe for ordinary shares, and meet the criteria to be classified as shareholders' equity (deficit). As such, following the final remeasurement on May 28, 2019, the Company reclassified the carrying value of the warrant liability to additional paid-in-capital in the consolidated balance sheet.

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 IPO, Bicycle Therapeutics Limited (for the purpose of the 2017 Reorganization referred to as "BTL NewCo."). These transactions are collectively referred to as the 2017 Reorganization. The 2017 Reorganization was enacted through a share-for-share exchange pursuant to which the shareholders of BTL OldCo. exchanged their shares for equivalent shares of BTL NewCo. Thereafter, 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, a newly created subsidiary of BTL NewCo. 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.

Liquidity

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.

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. Since inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital. The Company has funded its operations with proceeds from sales of convertible preferred shares (Note 6) and proceeds received from its collaboration arrangements (Note 10) and most recently, with proceeds from the IPO completed in May 2019. The Company has incurred recurring losses since inception, including net losses of $30.6 million for the year ended December 31, 2019, $21.8 million for the year ended December 31, 2018 and $16.3 million for the year ended December 31, 2017. As of December 31, 2019, the Company had an accumulated deficit of $100.6 million. The Company expects to continue to generate operating losses in the foreseeable future. As of March 10, 2020, the issuance date of the annual consolidated financial statements for the year ended December 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 annual consolidated financial statements.

The Company expects its expenses to increase substantially in connection with ongoing activities, particularly as the Company advances its preclinical activities and clinical trials for its product candidates in development. Accordingly, the Company will need to obtain additional funding in connection with continuing operations. If the Company is unable to raise capital when needed, or on attractive terms, it could be forced to delay, reduce or eliminate its research or drug development programs or any future commercialization efforts. Although management continues to pursue these plans, there is 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

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 the valuation of the warrant liability prior to the Company's IPO, share-based compensation expense, 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.

Foreign currency and currency translation

The functional currency is the currency of the primary economic environment in which an entity's operations are conducted. On June 1, 2019, Bicycle Therapeutics plc adopted the U.S. dollar as its functional currency. Bicycle Therapeutics plc is a holding company that has no operating activities and its primary functions are to serve as a financing vehicle to fund the operations of the Company's operating entities, to serve as the listing company needed to access U.S. capital markets, and to hold investments. Therefore, its financing source is the primary indicator of its cash flows and its functional currency. The change in functional currency from the British Pound Sterling is due to a change in the source of Bicycle Therapeutics plc's financing and cash flows, which following the completion of the IPO is now primarily the U.S. Dollar ("USD"). Historically its financing had been in British Pound Sterling.

The functional currency of Bicycle Therapeutics plc's wholly owned non-U.S. subsidiaries, BicycleTx Limited and BicycleRD Limited, is the British Pound Sterling and the functional currency of its U.S. subsidiary, Bicycle Therapeutics Inc. is the USD. 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 gain of $0.9 million, a foreign exchange gain of $0.3 million and a foreign exchange loss of $0.6 million and for the years ended December 31, 2019, 2018 and 2017, respectively.

The Company translates the assets and liabilities of 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' equity (deficit) as a component of accumulated other comprehensive 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 Sanofi (formerly 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, 2019, the Company's revenue to date has primarily been generated from the collaboration agreements with AstraZeneca, Sanofi, the Dementia Discovery Fund 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.

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, 2019 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, 2019 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' equity (deficit) 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.

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, 2019 and 2018, there have been no significant asset retirements to date. Expenditures for repairs and maintenance are charged to expense as incurred.

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.

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.

Prior to the IPO, the Company's warrant liability was 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.

Warrant liability

Prior to the IPO, the Company classified 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 were free-standing financial instruments that might have required the Company to transfer assets upon exercise. The warrant liability was initially recorded at fair value upon the date of the warrants' issuance and was subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant liability were recognized as a component of other expense, net in the consolidated statements of operations and comprehensive loss. Upon the closing of the IPO, warrants to subscribe for Series A and Series B1 convertible preferred shares that were not exercised or expired in conjunction with the IPO automatically became warrants to subscribe for ordinary shares, and meet the criteria to be classified as shareholders' equity (deficit). As such, following the final remeasurement on May 28,

2019, the Company reclassified the carrying value of the warrant liability to additional paid-in-capital in the consolidated balance sheet.

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.

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.

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 recognizes revenue in accordance with ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606) ("ASC 606") and all subsequent amendments. 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 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 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.

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"

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 year ended December 31, 2019, the Company recognized $0.6 million, as a reduction of research and development expense related to government grant arrangements. There were no grant proceeds recognized for the years ended December 31, 2018 or 2017.

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.

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 surrenderable 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 $6.7 million, $5.9 million and $2.9 million during the years ended December 31, 2019, 2018 and 2017, 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.

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, 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 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.

Prior to the IPO, the Company utilized significant estimates and assumptions in determining the fair value of its common stock. 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 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' equity (deficit) that result from transactions and economic events other than those with shareholders. The Company records unrealized gains and losses related to foreign currency translation as a component of other comprehensive loss in the consolidated statements of operations and comprehensive loss.

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 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.

Prior to the Company's IPO, convertible preferred shares contractually entitled 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 reported a net loss, such losses were not allocated to such preferred securities. In periods in which the Company reported 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 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 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, Massachusetts. 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.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles (Topic 350): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, which aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software. This standard also requires customers to amortize the capitalized implementation costs of a hosting arrangement that is a service contract over the term of the hosting arrangement. The Company early adopted this standard, as of April 1, 2019, on a prospective basis for applicable implementation costs. The adoption of this standard would not have had a material impact to historical accounting periods. The Company capitalized approximately $0.1 million of implementation cost for the year ended December 31, 2019.

Recently Issued Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, "Income Taxes: Simplifying the Accounting for Income Taxes," intended to simplify the accounting for income taxes by eliminating certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The standard is effective for annual periods beginning after December 15, 2020 and interim periods within, with early adoption permitted. Adoption of the standard requires certain changes to primarily be made prospectively, with some changes to be made retrospectively. We are currently assessing the impact of this standard on our financial condition and results of operations.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 will change how companies account for credit losses for most financial assets and certain other instruments. For trade receivables, loans and held-to-maturity debt securities, companies will be required to recognize an allowance for credit losses rather than reducing the carrying value of the asset. ASU 2016-13 is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2016-13 will have on the Company's financial position and results of operations.

3. Fair value of financial assets and liabilities

The warrant liability for warrants to subscribe for convertible preferred shares was initially recorded at fair value upon the date of the warrants' issuance and was subsequently remeasured to fair value at each reporting date (Note 7). Upon the closing of the IPO on May 28, 2019, warrants that were not exercised or expired in conjunction with the IPO automatically became warrants to subscribe for ordinary shares, and met the criteria to be classified as shareholders' equity (deficit). As such, following the final remeasurement on May 28, 2019, the Company reclassified the carrying value of the outstanding warrant liability to additional paid-in-capital in the consolidated balance sheet. As such, there is no warrant liability at December 31, 2019.

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

During the years ended December 31, 2019 and 2018, there were no transfers between levels.

4. Property and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2019	2018
Laboratory equipment	$ 4,326	$ 3,356
Leasehold improvements	300	75
Computer equipment and software	229	221
Furniture and office equipment	120	99
	4,975	3,751
Less: Accumulated depreciation and amortization	(2,683)	(1,933)
	$ 2,292	$ 1,818

Depreciation expense was $1.0 million, $0.7 million and $0.3 million for the years ended December 31, 2019, 2018 and 2017, respectively.

5. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2019	2018
Accrued employee compensation and benefits	$ 2,514	$ 1,610
Accrued external research and development expenses	2,055	3,814
Income taxes payable	1	15
Accrued professional fees	867	1,494
Current portion of operating lease liabilities	640	—
Other	67	99
	$ 6,144	$ 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.

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.

Upon the closing of the IPO in May 2019, all of the Company's outstanding convertible preferred shares automatically converted into 11,647,529 ordinary shares on a 1:1.429 basis.

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 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 28, 2019, in conjunction with the completion of the IPO, 120,000 warrants to subscribe for Series A Preferred Shares were exercised for 171,480 ordinary shares. The holders of the remaining 80,000 warrants provided the Company with an exercise delay notice, which are exercisable into 114,320 ordinary shares following the completion of the IPO, as adjusted for the impact of the Share Capital Reorganization (Note 1). As of December 31, 2019, 65,000 warrants are outstanding, which are exercisable into 92,885 ordinary shares.

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, 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, 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 would be exercised in conjunction with the IPO and 50% of the warrants would 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 expense for the year ended December 31, 2019. On May 28, 2019, in conjunction with the completion of the IPO, all Series B1 Preferred share warrants were exercised for 531,077 ordinary shares, as adjusted for the impact of the Share Capital Reorganization (Note 1).

Prior to the completion of the IPO, the warrants to subscribe for Series A and Series B1 Preferred Shares were recorded as a liability and remeasured to fair value at each reporting date (Note 3). Changes in the fair value of the warrant liability were recognized as other expense, net in the consolidated statements of operations and comprehensive loss. Upon the closing of the IPO on May 28, 2019, warrants that were not exercised in conjunction with the IPO automatically became warrants to subscribe for ordinary shares, and meet the criteria to be classified as shareholders'

equity (deficit). As such, following the final remeasurement on May 28, 2019, the Company reclassified the carrying value of the warrant liability to additional paid-in-capital in the consolidated balance sheet.

The following table provides a roll-forward of the fair values of the Company's warrant liability for which fair value was 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	5,381
Conversion of warrant liability to equity upon closing of IPO and exercise of warrants	(10,021)
Impact of exchange rates on translation of warrant liability to USD included in accumulated other comprehensive income (loss)	(164)
Fair value at December 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, prior to the IPO, 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 assessed these assumptions and estimates on a quarterly basis prior to the closing of the IPO in May 2019.

The quantitative elements associated with the Company's Level 3 inputs impacting the fair value measurement of the warrant liability included the fair value per share of the underlying Series A and Series B1 preferred shares or ordinary shares at the time of final remeasurement, into which the warrants were 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 was the fair value of the Series A and Series B1 preferred shares, or ordinary shares at the time of final remeasurement, into which the warrant is exercisable as of each remeasurement date. Given the absence of an active market for the Company's equity securities prior to the IPO, the Company determined 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, risk-free interest rate, expected dividend yield and expected volatility did not have an impact to the fair value of the warrants because the exercise price of the warrants was £0.01, and the fair value of the warrant was equal to the difference between the exercise price and the fair value regardless of the assumptions. The Company historically had been a private company and lacked company-specific historical and implied volatility information of its shares. Therefore, it estimated 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 was 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 had 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:

	Remeasurement upon closing of the IPO on May 28, 2019		December 31, 2018	
	Series A Warrants	Series B1 Warrants	Series A Warrants	Series B1 Warrants [1]
Risk-free rate	2.2 %	2.1 %	2.6 %	2.5 %
Expected dividend yield	— %	— %	— %	— %
Expected term (years)	8.0	5.8	8.4	6.25
Expected volatility	74.7 %	78.2 %	75.4 %	79.6 %
Exercise price	£ 0.01	£ 0.01	£ 0.01	£ 0.01
Fair value of preferred shares or ordinary shares underlying the warrant	$ 12.28	$ 12.28	$ 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.

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, 2019 and 2018, the Company has not declared any dividends.

As of December 31, 2019 and 2018, the Company's authorized capital share consisted of 31,995,653 and 15,452,420 ordinary shares, respectively, with a nominal value of £0.01 per share.

9. Share-based compensation

Employee incentive pool

2019 Share Option Plan

In May 2019, the Company adopted the 2019 Share Option Plan (the "2019 Plan"), which became effective in conjunction with the IPO. In September 2019, the Compensation Committee of the Company's Board of Directors approved immaterial clarifying amendments to the 2019 Plan which did not have an impact to the consolidated financial statements. The 2019 Plan provides for the grant of options to purchase ordinary shares and other share-based awards to officers, employees, directors and other key persons (including consultants).

The Company has initially reserved 2,470,583 ordinary shares for future issuance under the 2019 Plan. The number of ordinary shares reserved for issuance of the 2019 Plan will automatically increase on the first day of January, commencing on January 1, 2020, in an amount equal to 4% of the total number of ordinary shares outstanding on the last day of the preceding year, or a lesser number of shares determined by the Company's board of directors, subject to adjustment in the event of a share split, share dividend or other change in capitalization. As of December 31, 2019, there were 872,646 shares available for issuance under the 2019 Plan. The number of shares reserved for issuance under the 2019 Plan was increased by 719,748 shares effective January 1, 2020.

Share options issued under the 2019 Share Option Plan have a 10 year contractual life, and either vest monthly over a three year service period, or 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 installments. The exercise price of share options issued under the 2019 Share Option Plan shall not be less than the fair value of ordinary shares as of the date of grant.

Pre-IPO Share Options and restricted shares

Prior to the IPO, the Company issued share options and ordinary shares, as administered by the board of directors, using standardized share option and share subscription agreements. To the extent such incentives were 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. Upon completion of the IPO, shares reserved for future issuance outside of the 2019 Share Option Plan were cancelled.

Options granted, as well as restricted shares granted as employee incentives prior to the IPO, 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 installments and expire no later than 10 years from the date of grant.

Certain equity awards were issued in 2017 and 2018 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 issued to U.K. employees prior to the IPO generally had an exercise price of £0.01 per share. The exercise price for share options granted to U.S. employees, had an exercise price that was not less than the fair value of ordinary shares as determined by the board of directors as of the date of grant. Prior to the IPO, the Company's board of directors valued 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.

Employee Share Purchase Plan ("ESPP")

In May 2019, the Company adopted the 2019 Employee Stock Purchase Plan ("ESPP"), which became effective in conjunction with the IPO. The Company initially reserved 215,000 ordinary shares for future issuance under this plan. Each offering to the employees to purchase shares under the ESPP will begin on each June 1 and December 1 and will end on the following November 30 and May 31, respectively. On each purchase date, which falls on the last date of each offering period, ESPP participants will purchase ordinary shares at a price per share equal to 85% of the lesser of (1) the fair market value of the shares on the offering date or (2) the fair market value of the shares on the purchase date. The occurrence and duration of offering periods under the ESPP are subject to the determinations of the Company's compensation committee. As of December 31, 2019, there have been no offering periods to employees under ESPP.

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,		
	2019	2018	2017
Research and development expenses	$ 1,286	$ 513	$ 241
General and administrative expenses	1,797	510	274
	$ 3,083	$ 1,023	$ 515

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 (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2018	863,712	$ 1.01	8.75	$ 3,292
Granted	2,134,538	12.01	—	—
Exercised	(85,839)	1.67	—	—
Forfeited	(278,065)	4.21	—	—
Outstanding as of December 31, 2019	2,634,346	$ 9.57	9.04	$ 6,107
Vested and expected to vest as of December 31, 2019	2,634,346	$ 9.57	9.04	$ 6,107
Options exercisable as of December 31, 2019	647,901	$ 6.81	8.49	$ 2,868

The weighted average grant-date fair value of share options granted during the years ended December 31, 2019, 2018 and 2017 was $6.07 per share, $3.73 per share and $1.78 per share, respectively.

For the years ended December 31, 2019, 2018 and 2017, the Company recorded share-based compensation expense for share options granted of $2.7 million, $0.8 million and $0.4 million, respectively. Expense for non-employee consultants for the years ended December 31, 2019, 2018 and 2017, 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, 2019, 2018 and 2017 was $0.6 million, $23,000 and $7,000 respectively.

During the year ended December 31, 2019, 2018 and 2017, the Company granted certain performance based vesting options for the purchase of an aggregate of zero, 70,875 and 678,610 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. 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 $0.1 million, $0.7 million and $0.3 million, during the year ended December 31, 2019, 2018 and 2017, 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,		
	2019	2018	2017
Risk-free interest rate	2.1 %	2.7 %	2.0 %
Expected volatility	77.9 %	78.6 %	79.7 %
Expected dividend yield	—	—	—
Expected term (in years)	5.86	6.07	6.07

As of December 31, 2019, total unrecognized compensation expense related to the unvested employee and director share-based awards was $10.6 million, which is expected to be recognized over a weighted average period of 2.5 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.

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	(83,947)	1.93
Unvested restricted ordinary shares as of December 31, 2019	—	$ —

In conjunction with the IPO in May 2019, the board of directors modified the vesting terms to accelerate vesting for all then unvested restricted shares. As a result, the Company recorded $0.2 million of expense upon the modification of the restricted shares during the year ended December 31, 2019.

For the years ended December 31, 2019, 2018 and 2017, the Company recorded share-based compensation of $0.4 million, $0.2 million, and $0.1 million, respectively, for unvested restricted shares granted.

The fair value of employee restricted share awards vested during the years ended December 31, 2019, 2018 and 2017, based on estimated fair values of the ordinary shares underlying the restricted share awards on the day of vesting, was $0.7 million, $0.2 million and $0.1 million, respectively.

As of December 31, 2019, there was no unrecognized compensation cost related to the unvested employee and director restricted share awards.

10. Significant Agreements

For the years ended December 31, 2019, 2018 and 2017, the Company had collaboration agreements with AstraZeneca, Sanofi, (formerly Bioverativ), Oxurion (formerly ThromboGenics) and the Dementia Discovery Fund. 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,		
	2019	2018	2017
Collaboration revenues			
AstraZeneca	$ 1,683	$ 1,386	$ 890
Sanofi	10,724	4,007	355
Oxurion	—	1,743	815
Dementia Discovery Fund	394	—	—
Material transfer agreement	1,000	—	—
Total collaboration revenues	$ 13,801	$ 7,136	$ 2,060

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 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").

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 years ended December 31, 2019, 2018 and 2017 the Company recognized $0.2 million, $1.0 million, and $0.9 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, 2019 and 2018, the Company recorded zero deferred revenue, and $8,000 of deferred revenue, respectively, in connection with the 2016 AstraZeneca Collaboration Agreement.

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 in January 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 the Company 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.

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 initially 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. 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 and, therefore, are not considered performance obligations and are accounted for as separate contracts. In June 2019, AstraZeneca selected a replacement target for the third target, and as such a new Research Term was started related to the Target Three Research License and Related Services. The total transaction price under the arrangement increased to $6.3 million for the additional research and development funding to be received. During the year ended December 31, 2019, the Company commenced research and development services related to the fourth and fifth targets.

For the year ended December 31, 2019, 2018 and 2017, the Company recognized $1.5 million, $0.4 million, and zero, respectively, of revenue related to the Target Three Research License and Related Service, and research and development services for the fourth target and fifth target related to the May 2018 AstraZeneca Option Exercise. As of

December 31, 2019 and 2018, the Company recorded $4.9 million and $4.7 million, respectively, of deferred revenue in connection with the May 2018 AstraZeneca Option Exercise and related contracts.

Sanofi Collaboration Agreement (formerly Bioverativ)

Summary of Agreement

In August 2017, the Company entered into a Collaboration Agreement with Bioverativ Inc., which was acquired by Sanofi in March 2018 ("Sanofi"). Under the collaboration agreement with Sanofi (the "Sanofi Collaboration Agreement"), the Company was obligated to provide 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 used its bicyclic peptide screening platform to perform research and development services for the programs and Sanofi had 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 Sanofi Collaboration Agreement, the Company was 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 was 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, Sanofi could, 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, Sanofi was required to pay an option fee. During the Joint Research Term, the Company and Sanofi would jointly conduct research and development activities which included lead optimization of lead compounds, in preparation for lead collaboration product nomination ("Joint Research Term"). Sanofi could, at its sole discretion, approve any compound to be progressed into drug development and upon the selection of each collaboration product candidate, Sanofi was obligated to pay $5.0 million as an option fee, in order to obtain worldwide development and exploitation rights for that collaboration product.

Each research program had an initial period of three years (the "Research Term") unless a program was abandoned by Sanofi or extended for up to one year. The first year of each Research Term was the BV Bicycle Research Term and the remaining part of the Research Term, including any extensions of the Research Term, was the Joint Research Term.

Under the terms of the Sanofi Collaboration Agreement, the Company granted to Sanofi, 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 Sanofi in the applicable research plan for the duration of the applicable Research Term, but for no other purpose.

The activities under the Sanofi Collaboration Agreement were governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and Sanofi. The JSC oversaw, reviewed and recommend direction of each collaboration program and variations of or modifications to the research plans.

Under the terms of the Sanofi 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, Sanofi 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, Sanofi was 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. Sanofi had 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, Sanofi was 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 was 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 was eligible for up to $55.0 million in commercial milestone payments, on a research program by

research program basis. Development milestone payments were triggered upon initiation of a defined phase of clinical research for a collaboration product. Regulatory milestone payments were triggered upon approval to market a product candidate by the FDA or other global regulatory authorities. Commercial milestone payments were 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 Sanofi were 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 were subject to certain reductions, including for instances where Sanofi faces generic competition in certain countries.

Under the terms of the Collaboration Agreement, Sanofi 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 could terminate the Sanofi Collaboration Agreement if the other party had 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 could terminate the Sanofi 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. Sanofi could terminate the Sanofi 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.

Accounting Analysis

The Company identified the following four performance obligations associated with the Sanofi 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 was not a material right, as the option did not provide a discount that Sanofi 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 were not performance obligations at the inception of the arrangement, as they were optional services to be performed if Sanofi selected collaboration compounds for lead optimization. The amount paid by Sanofi for the services during the Joint Research Team did not reflect a discount that the customer would otherwise receive and did 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 could 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 were excluded from the transaction price as they related to fees and milestones that could 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 was 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 Sanofi 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 Sanofi. Based on the relative standalone selling price, the allocation of the transaction price to the separate performance obligations was 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 recognized revenue related to amounts allocated to the Sickle Cell and Hemophilia Research License and Related Services obligations as the underlying services were 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 reflected the progress towards satisfaction of the performance obligation. The amount allocated to the material rights was recorded as deferred revenue, and the Company commenced revenue recognition when the underlying option was exercised or upon expiry of the option.

During the year ended December 31, 2019, Sanofi extended the research and development services on both programs. The arrangement consideration increased to $14.9 million. On March 28, 2019, Sanofi notified the Company that it would not exercise the Sickle Cell License Option. In addition, the collaboration with Sanofi was terminated effective October 23, 2019. As a result, deferred revenue related to amounts allocated to the Sickle Cell License Option Material Right of $5.3 million and the Hemophilia License Option Material Right of $4.7 were recognized during the year ended December 31, 2019. For the years ended December 31, 2019, 2018 and 2017, the Company recognized $10.7 million, $4.0 million and $0.4 million, respectively, of collaboration revenue related to its collaboration with Sanofi. As of December 31, 2019 and 2018, the Company recorded deferred revenue of zero and $9.9 million, respectively, related to its collaboration with Sanofi, 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.

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, 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. 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 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, 2019 and December 31, 2018.

For the years ended December 31, 2019, 2018 and 2017, the Company recognized zero, $1.7 million and $0.8 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 years ended December 2019, 2018 and 2017 includes zero, $1.2 million and $0.8 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, 2019 and 2018 in connection with the agreements with Oxurion.

Dementia Discovery Fund Agreement

In May 2019, the Company entered into a collaboration with the Dementia Discovery Fund (“DDF”) to use Bicycle technology for the discovery and development of novel therapeutics for dementia (the “DDF Collaboration

Agreement"). In October 2019, the collaboration with DDF was expanded to include Oxford University's Oxford Drug Discovery Institute (ODDI). Under the terms of the DDF Collaboration Agreement, the Company and DDF will collaborate to identify *Bicycles* that bind to clinically validated dementia targets (the "DDF Research Plan"). The Company is obligated to use commercially reasonable efforts to perform research activities under the DDF Research Plan. DDF shall not be directly engaged in the conduct of any research activities under the arrangement. ODDI will then profile these *Bicycles* in a range of target-specific and disease-focused assays to determine their therapeutic potential. The activities under the DDF Collaboration Agreement will be governed by a project advisory panel, composed of two representatives from the Company and DDF. The Research Advisory Panel will oversee, review and recommend direction for the Research Plans and variations of or modifications of research plans.

The Company received an upfront payment of $1.1 million in May 2019. The Company may receive up to an additional $0.7 million, upon achievement of certain milestones such as the identification of lead bicycle candidates with a certain affinity, which would be used to fund additional research and development services including lead optimization.

Intellectual property created by the collaboration shall be owned by the Company, and background intellectual property improvements shall be owned by the party from whose background intellectual property they exclusively relate. If promising lead compounds are identified, the Company, ODDI and DDF have the option (the "DDF Option") to establish a jointly owned new company ("NewCo") to advance the compounds through further development towards commercialization. NewCo will receive a royalty and milestone-bearing assignment and license of intellectual property from the Company for this purpose. The DDF Option is exercisable at any time until 90 days following the completion of the Research Plan and delivery of a final report. If DDF does not elect to exercise the DDF Option during the Option period, then DDF shall have no right in the collaboration intellectual property. NewCo will initially be owned 66% by the Company and 34% by DDF; however, the Company shall not be entitled to exercise more than 50% of the total voting rights related to its ownership interests. After completion of the DDF Option exercise, for a period of two years following the option exercise, NewCo shall have the right to initiate a new research program to develop up to three additional dementia targets, on a target by target basis, and the Company will be entitled to charge NewCo an agreed upon FTE rate for peptide screening and optimization for the active targets.

Either party may terminate the DDF Collaboration Agreement upon providing not less than 60 days written notice. A party may terminate the DDF Collaboration Agreement with immediate effect without notice if at any time the other party files for protection under bankruptcy or insolvency laws, makes an arrangement for the benefit of creditors, appoints a receiver, administrator, manager or trustee over its property, proposes a written agreement of composition or extension of its debts, is a party to any dissolution, winding-up or liquidation, or is in material breach that has not been remedied.

Accounting Analysis

The Company identified a single performance obligation associated with the performance of research and development services under the DDF Research Plan.

The Company concluded that the DDF Option is an immaterial obligation at the inception of the arrangement, as it represents a right to acquire shares of NewCo that have *de minimis* value. The DDF Option also does not contain a material right that otherwise would not have been received. The Company's participation in the Research Advisory Panel was assessed as immaterial in the context of the contract. In addition, the Company concluded that the option for NewCo to obtain additional peptide screening and optimization services is not an obligation at the inception of the arrangement, as they are optional services and the amount that will be paid for the services 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 $1.1 million, consisting of the upfront payment for research and development funding. The Company may receive additional milestone payments during the DDF Research Plan, as well as for research and development services for additional targets following the exercise of DDF Option. These variable amounts are excluded from the transaction price as they relate to fees that can only be achieved subsequent to the exercise of an option.

The transaction price was allocated to the single performance obligation of research and development services. The Company will recognize revenue as the underlying services are performed using a proportional performance model, over the period of service using input-based measurements of total costs, including total full-time equivalent effort incurred to date as a percentage of total costs expected, which best reflects the progress towards satisfaction of the performance obligation.

For the year ended December 31, 2019, the Company recognized $0.4 million of revenue, and recorded deferred revenue of $0.7 million for the year ended December 31, 2019 related to its collaboration with DDF.

Material Transfer Agreement

In October 2018, the Company entered into a Materials Transfer Agreement. Under the terms of the agreement, the Company agreed to transfer bicyclic peptides (the "Materials") to the recipient for the purpose of testing the materials in order to evaluate the Company's technology platform. The recipient agreed to pay the Company $1.0 million within 30 business days after receipt of the materials and related data package, which was paid to the Company in May 2019. The agreement has a term of 14 months after delivery of the Materials and data package and may be terminated upon 45 days' notice by the recipient. At any point during the term of the agreement and continuing through two months after the completion of the permitted research, the recipient has the option to enter into good faith negotiations to obtain a license to the Company's background intellectual property and/or the Company's interest in the new substances or developments for the purpose of continued research and development of collaboration products.

For the year ended December 31, 2019 and 2018, the Company recognized $1.0 million and zero, respectively, of revenue related to its Materials Transfer Agreement, as the Company concluded that the recipient has the ability to direct the use of and obtain substantially all of the remaining benefit from the Materials upon the delivery of the Materials and the data package.

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.

	Balance at Beginning of Period	Additions	Deductions	Impact of Exchange Rates	Balance at End of Period
Period ended December 31, 2019					
Contract assets	$ —	$ 149	$ (149)	$ —	$ —
Contract liabilities:					
Deferred revenue					
AstraZeneca collaboration deferred revenue	4,727	58	(35)	163	4,913
Sanofi collaboration deferred revenue	9,908	—	(9,984)	76	—
DDF collaboration deferred revenue	—	1,114	(394)	24	744
Total deferred revenue	$ 14,635	$ 1,172	$ (10,413)	$ 263	$ 5,657

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					
AstraZeneca collaboration deferred revenue	—	5,350	(466)	(157)	4,727
Sanofi collaboration deferred revenue	14,467	—	(4,006)	(553)	9,908
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 AstraZeneca deferred revenue balance as of December 31, 2019 includes $4.9 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, 2019, 2018 and 2017, 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,		
	2019	2018	2017
Revenue recognized in the period from:			
Revenue recognized based on proportional performance	$ (429)	$ (4,472)	$ (355)
Revenue recognized based on expiration of material rights	(9,984)	—	—
Total	$ (10,413)	$ (4,472)	$ (355)

Cancer Research UK

BT1718

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 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 CRTL may elect to receive an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case the Company will receive tiered royalties of 70% to 90% 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 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 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 CRT may elect to receive 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 Developmen*t, as the payment is not based solely on the results of the research and development having future economic benefit. As such, for the year ended December 31, 2019 and 2018, the Company recorded a liability of $2.0 million and $0.8 million, 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.

BT7401

In December 2019, the Company entered into a clinical trial and license agreement with the Cancer Research Technology Limited and CRUK. Pursuant to the agreement, CRUK's Centre for Drug Development will fund and sponsor development of BT7401 from current preclinical studies through the completion of a Phase IIa trial in patients with advanced solid tumors.

The Company granted to CRUK a license to our intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial and all necessary preclinical activities to support the trial. The Company retains the right to continue the development of BT7401 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 contain BT7401 or all the pharmaceutically active parts of BT7401, the Cancer Research Technology Limited may elect to receive an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case the Company will receive tiered royalties of 55% to 80% 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, with an aggregate total value of up to $60.3 million for each licensed product, as well as royalty payments based on a single

digit percentage on net sales of products developed, and sublicense royalties to the CRUK in the very low double digit percentage of sublicense income depending on the stage of development when the license is granted.

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 upon written notice by either party prior to the last cycle of treatment has been completed under the clinical trial. If the study is terminated by the Company prior to the filing of a clinical trial authorization, or by the CRUK for an insolvency event or a material breach by us prior to the start of a clinical trial, the Company will reimburse CRUK for certain costs paid or committed prior to the start of the clinical trial. In such case where the Company is 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 the Cancer Research Technology Limited may elect to receive an exclusive license to develop and commercialize the product without Cancer Research Technology Limited being required to make any payment to the Company. There were no activities initiated under the BT7401 CRUK arrangement as of December 31, 2019, and as such there was no accounting impact as of and for the year ended December 31, 2019.

11. Income Taxes

The components of net loss before tax provision from income taxes are as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
United Kingdom	$(31,906)	$(22,229)	$(16,319)
United States	1,044	(13)	37
Total	$(30,862)	$(22,242)	$(16,282)

The components of the benefit for income taxes are as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Current income tax provision (benefit)			
Federal	$ 49	$ (25)	$ 75
State	61	7	10
Total current income tax provision (benefit)	110	(18)	85
Deferred income tax (benefit) provision			
Federal	(295)	(167)	(58)
State	(69)	(211)	(50)
Total deferred income tax (benefit)	(364)	(378)	(108)
Total benefit from income taxes	$ (254)	$ (396)	$ (23)

A reconciliation of the benefit for income taxes computed at the statutory income tax rate to the benefit for income taxes as reflected in the financial statement is as follows:

	Year Ended December 31,		
	2019	2018	2017
Benefit for income taxes at statutory rate	19.0 %	19 %	19 %
(Decreases) increases resulting from:			
Federal tax credits	1.3 %	1.1 %	0.4 %
Change in valuation allowance	(8.0)%	(7.2)%	(9.4)%
Net losses surrendered for research credit	(5.3)%	(3.7)%	(6.7)%
Preferred share warrants	(3.3)%	(0.6)%	(1.1)%
Other	(2.9)%	(6.8)%	(2.1)%
Effective income tax rate	0.8 %	1.8 %	0.1 %

Significant components of the Company’s current and deferred tax assets at December 31, 2019 and 2018, were as follows (in thousands):

	Year Ended December 31,	
	2019	2018
Deferred tax assets:		
Operating loss carryforwards	$ 7,082	$ 4,953
Research credit carryforwards	434	197
Operating lease liability	439	—
Accrued expenses and other	1,779	1,149
Total deferred tax assets	9,734	6,299
Deferred tax liabilities:		
Operating lease right-of-use asset	(422)	—
Depreciation & amortization	(326)	(163)
Total deferred tax liabilities	(748)	(163)
Valuation allowance	(8,104)	(5,621)
Net deferred tax assets	$ 882	$ 515

During the years ended December 31, 2019, 2018 and 2017, the Company recorded an income tax benefit of $0.3 million, $0.4 million and $23,000, 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 therefore not paid United Kingdom corporation tax. The Company's income tax benefit is mainly the result of deferred tax assets benefited 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 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 States deferred tax assets and has not provided a valuation allowance against the net deferred tax assets in the United States. The valuation allowance increased in the year ended December 31, 2019 by $2.5 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, 2019 and 2018.

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, 2019, the Company had $41.7 million of U.K. operating loss carryforwards and zero of federal and state net operating loss carryforwards. 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. As of December 31, 2019, the Company had $0.3 million and $0.2 million of federal and state research and development credit carryforwards, respectively, that expire at various dates through 2039.

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, 2019 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 ordinary course of business, the Company is subject to examination by tax authorities in these jurisdictions. The 2017 and 2018 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 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. 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 2017 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 ASU 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.

The future minimum lease payments due under the Company's operating leases as of December 31, 2018 under ASC 840 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 year ended December 31, 2018 and 2017 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 year ended December 31, 2018 and 2017, the Company recognized total rent expense of $1.0 million and $0.5 million, respectively.

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 square 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.

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 consolidated statement of operations and comprehensive loss are as follows (in thousands):

	December 31, 2019
Operating lease cost	$ 900
Variable lease cost	390
Total lease cost	$ 1,290
Weighted-average remaining operating lease term (years)	2.6
Weighted-average discount rate	8.52 %

Future minimum lease payments under non-cancelable operating leases under ASC 842 as of December 31, 2019 are as follows (in thousands):

Year Ending December 31,	
2020	$ 879
2021	777
2022	443
2023	—
2024	—
Present value adjustment	(208)
Total lease liabilities	$ 1,891
Less: current lease liabilities	(640)
Long term lease liabilities	$ 1,251

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.

In September 2016, the Company's subsidiary, BicycleRD, filed a complaint in the District Court of the Hague against Pepscan Systems B.V. and its affiliates ("Pepscan") to contest the right of Pepscan to terminate a non-exclusive patent license agreement entered into with Pepscan in 2009 ("PLA"). BicycleRD included a conditional claim for a ruling that the licensed patent relevant to BicycleRD's activities is invalid. 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, 2019 or 2018. 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. 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, 2019 and 2018.

13. 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,		
	2019	2018	2017
Numerator:			
Net loss attributable to ordinary shareholders	$ (30,608)	$ (21,846)	$ (16,259)
Denominator:			
Weighted average ordinary shares outstanding, basic and diluted	11,045,370	438,862	333,125
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (2.77)	$ (49.78)	$ (48.81)

The Company's potentially dilutive securities, which include share options, warrants to subscribe for ordinary shares, and which prior to the completion of the IPO, included convertible preferred shares, 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,		
	2019	2018	2017
Convertible preferred shares (as converted to ordinary shares)	—	11,532,659	9,641,740
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)(2)	92,885	1,347,953	1,347,953
Restricted ordinary shares	—	83,947	162,466
Options to purchase ordinary shares	2,634,346	863,712	964,538
	2,727,231	13,828,271	12,116,697

(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 would be exercised in conjunction with the IPO and 50% of the warrants would expire.

(2) At December 31, 2019 65,000 warrants are outstanding which are exercisable into 92,885 ordinary shares (Note 6).

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, 2019, 2018, and 2017 the Company made contributions totaling $0.2 million, $0.1 million and $42,000, 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, 2019, 2018 and 2017 the Company made contributions totaling $0.3 million, $0.2 million and $0.2 million, respectively, to the U.K. Plan.

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 Stone Sunny Isles Inc., which provided consultancy services to the Company totaling $0.1 million during the year ended December 31, 2019.

The former Chairman of the Company's Board of Directors is associated with 10X Capital Inc., which provided consultancy services to the Company totaling $50,000, $0.2 million, and $0.1 million during the years ended December 31, 2019, 2018 and 2017, 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, 2019	December 31, 2018
United States	$ 2,017	$ 498
United Kingdom	2,331	1,320
	$ 4,348	$ 1,818

The Company's collaboration revenues are attributed to the operations of the Company in the United Kingdom.

17. Selected Quarterly Financial Data (Unaudited)

The following tables contain selected quarterly financial information for 2019 and 2018. The Company believes the following information includes all recurring adjustments necessary for a fair statement of such information (in thousands, except share and per share data):

	Three Months Ended December 31, 2019	September 30, 2019	June 30, 2019	March 31, 2019
Statements of Operations Data:				
Collaboration revenues	$ 5,281	$ 614	$ 1,522	$ 6,384
Total operating expenses	10,045	10,867	9,510	9,678
Total other income (expense), net	220	440	(2,094)	(3,129)
Net loss before income tax provision	(4,544)	(9,813)	(10,082)	(6,423)
(Benefit from) provision for income taxes	(138)	(331)	135	80
Net loss	$ (4,406)	$ (9,482)	$ (10,217)	$ (6,503)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (0.25)	$ (0.53)	$ (1.40)	$ (7.80)
Weighted average ordinary shares outstanding, basic and diluted	17,926,165	17,900,978	7,298,139	834,043

	Three Months Ended December 31, 2018	September 30, 2018	June 30, 2018	March 31, 2018
Statements of Operations Data:				
Collaboration revenues	$ 1,057	$ 1,610	$ 1,661	$ 2,808
Total operating expenses	8,599	7,967	6,619	5,697
Total other expense, net	901	(1,335)	(21)	(41)
Net loss before income tax provision	(6,641)	(7,692)	(4,979)	(2,930)
Benefit from income taxes	—	—	—	(396)
Net loss	$ (6,641)	$ (7,692)	$ (4,979)	$ (2,534)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (13.19)	$ (17.73)	$ (11.85)	$ (6.38)
Weighted average ordinary shares outstanding, basic and diluted	503,309	433,795	420,063	397,483

18. Subsequent events

On February 21, 2020, the Company entered into a Discovery Collaboration and License Agreement (the "Genentech Collaboration Agreement") with Genentech, a member of the Roche Group. The collaboration is focused on the discovery and development of *Bicycle* peptides directed to biological targets selected by Genentech and aimed at developing up to four potential development candidates against multiple immuno-oncology targets suitable for Genentech to advance into further development and commercialization. Bicycle will be responsible for discovery and lead optimization of such *Bicycle* peptides through specified phases of the collaboration, and following drug candidate selection Genentech will be responsible for all future research and development. The initial discovery and optimization activities will focus on two immuno-oncology targets, potentially with additional targeting elements, and Genentech has the option to nominate up to two additional immuno-oncology targets, potentially with additional targeting elements, to be the subject of additional collaboration programs during a specified period following completion of certain activities under an agreed research plan, in which case Genentech will pay to the Company an expansion fee of $10.0 million per additional collaboration program. Genentech has the right, under certain limited circumstances, to select an alternative target to be the subject of a collaboration program, in some cases subject to payment of an additional target selection fee.

Under the Genentech Collaboration Agreement, Genentech will make an upfront payment to the Company of $30.0 million. The Company will perform research activities for each target under the collaboration, under a mutually agreed upon research plan through specified collaboration phases, under the oversight of a joint research committee. For each collaboration program, Genentech may elect, at its sole discretion, to progress development candidates into further preclinical development and obtain exclusive worldwide development and commercialization rights for compounds directed to the target of such collaboration program in exchange for success-based milestone payments totaling $10-12 million per collaboration program.

On a collaboration program-by-collaboration program basis, if Genentech elects to obtain exclusive development and commercialization rights and pays the applicable success-based milestone payments, Genentech will be required to make milestone payments to the Company upon the achievement of specified development, regulatory, and initial commercialization milestones for products arising from each collaboration program, totaling up to $200.0 million. In addition, the Company is also eligible to receive up to $200.0 million in sales milestone payments on a product-by-product basis. In addition, to the extent any of the product candidates covered by the licenses conveyed to Genentech are commercialized, the Company would be entitled to receive tiered royalty payments on net sales at percentages ranging from the mid-single to low double-digits, subject to certain standard reductions and offsets. Royalties will be payable, on a product-by-product and country-by-country basis, until the later of the expiration of specified licensed patents covering such product in such country, or ten years from first commercial sale of such product in such country.

Either party may terminate the Genentech Collaboration Agreement for the uncured material breach of the other party or in the case of insolvency. Genentech may terminate the Genentech Collaboration Agreement for convenience on specified notice periods depending on the development stage of the applicable program, either in its entirety or on a program-by- program basis or major market-by-major market basis.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Company has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Bicycle Therapeutics plc

Dated: March 10, 2020

/s/ Kevin Lee
Kevin Lee, Ph.D., MBA
Chief Executive Officer (Principal Executive Officer)

/s/Lee Kalowski
Lee Kalowski, MBA
Chief Financial Officer and President (Principal Financial and Accounting Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Kevin Lee and Lee Kalowski, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report on Form 10-K has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Kevin Lee Kevin Lee, Ph.D., MBA	Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2020
/s/ Lee Kalowski Lee Kalowski, MBA	Chief Financial Officer and President (Principal Financial and Accounting Officer)	March 10, 2020
/s/ Pierre Legault Pierre Legault, MBA, CPA	Chairman of the Board and Director	March 10, 2020
/s/ Michael Anstey Michael Anstey, DPhil	Director	March 10, 2020
/s/ Catherine Bingham Catherine Bingham, MBA	Director	March 10, 2020
/s/ Janice Bourque Janice Bourque, MBA	Director	March 10, 2020
/s/ Bosun Hau Bosun Hau	Director	March 10, 2020
/s/ Veronica Jordan	Director	March 10, 2020

Veronica Jordan, Ph.D.		
/s/ Richard Kender Richard Kender, MBA	Director	March 10, 2020
/s/ Carolyn Ng Carolyn Ng, Ph.D.	Director	March 10, 2020
/s/ Sir Gregory Winter Sir Gregory Winter, FRS	Director	March 10, 2020

Exhibit 4.4

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following describes certain material terms and provisions of the ordinary shares with nominal value of £0.01 per share of Bicycle Therapeutics plc ("Bicycle," the "company," "we," "our," or "us") which are represented by American Depositary Shares ("ADSs") with each ADS representing one ordinary share that are registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The description summarizes relevant provisions of English law, including the U.K. Companies Act 2006 (the "Companies Act"). The following summary does not purport to be complete and is subject to, and is qualified in its entirety by reference to, the applicable provisions of English law and our articles of association, a copy of which is filed as an exhibit to the Annual Report on Form 10-K. We encourage you to read our articles of association and the applicable provisions of English law for additional information.

General

We were incorporated pursuant to the laws of England and Wales as Bicycle Therapeutics Limited on October 27, 2017 and re-registered as a public limited company named Bicycle Therapeutics plc on May 22, 2019. 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 were passed by our shareholders in connection with our initial public offering, including a special resolution approving the adoption of new articles of association that became effective upon the admission of our ADSs to trading on Nasdaq.

Issued Share Capital

Effective from May 13, 2019, the board of directors has the authority to allot new ordinary shares or to grant rights to subscribe for or to convert any security into ordinary shares in the company up to a maximum aggregate nominal amount of £150,000. This authority runs for five years and will expire on May 13, 2024. This is in addition to the specific authorities to allot new ordinary shares or grant rights to subscribe for new ordinary shares in relation to our equity plans. In addition, statutory preemption rights were disapplied in respect of new ordinary shares issued or rights to subscribe for new ordinary shares granted pursuant to such authorities.

As of December 31, 2019, the company's issued share capital consisted of 17,993,701 ordinary shares, with a nominal value of £0.01 per share. Each issued share has been fully paid.

Ordinary Shares

Our ordinary shares have the rights and restrictions described in "Key Provisions of Our Articles of Association" below. 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, Computershare Investor Services plc.

Holders of our ADSs are not treated as one of our shareholders and their names are therefore not 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."

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 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 share register; 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 disapplication 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 disapplication would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). On May 13, 2019, our shareholders approved the disapplication of preemptive rights for a period of five years from the date of approval in relation to the shares authorised to be allotted pursuant to such resolutions, which disapplication 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).

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.

As 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.

Under our articles of association, if a shareholder defaults in supplying the company with the required details in relation to the shares in question, or the default shares within the prescribed period our board of directors may by notice direct that:

- the relevant shareholder shall not be entitled in respect of the default shares to be present or vote, either in person or by proxy, at any general meeting or separate meeting of the holders of a class of shares or upon any poll or to exercise any other right conferred by the membership in relation to any such meeting;
- where the default shares represents at least 0.25% of the issued shares of the class in question, (a) any dividend or other money payable in respect of the default shares shall be retained by us without any liability to pay interest, and/or (b) no transfers by the relevant shareholder of default shares (other than a transfer approved in accordance with the provisions of the company's articles of association) may be registered, unless the shareholder himself or herself is not in default and the shareholder proves to the satisfaction of the board of directors that no person in default as regards to supplying such information is interested in any of the default shares; and/or
- any shares held by the relevant shareholder in uncertificated form shall be converted into certificated form.

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.

The Nasdaq Global Market 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.

Registration Rights

Certain holders of our ordinary shares are 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 shares. The registration rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights.

Demand Registration Rights

Certain holders of our ordinary shares 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 our initial public offering and (iii) such time as all relevant ordinary shares may be sold pursuant to rule 144 during a 90-day period without registration.

Key Provisions of Our Articles of Association

Our articles of association were approved by our shareholders in May 2019 and were effective following the completion of our initial public offering in May 2019. A summary of certain key provisions of our articles of association is set out below. The summary below is not a complete copy of the provisions of the Articles. For further information please refer to the full version of our articles of association, which is included as an exhibit to this Annual Report on Form 10-K.

The articles of association 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 of association contain, among other things, provisions to the following effect:

Share Capital

Our share capital consists 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. Subject to any other provisions of our articles of association and without prejudice to any special rights, privileges or restrictions as to voting attached to any shares forming part of our share capital, 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 shareholder 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 (i) with the consent in writing of the holders of three-quarters in nominal value of the issued shares of that class, (ii) with the authority of a special resolution passed at a general meeting of the holders of the shares of that class or (iii) in any other way as expressly provided for in relation to such rights, 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 irrespective of the amount paid or credited as paid on any share.

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 in such manner provided for, and subject as provided in, the uncertificated securities rules (as defined in our articles of association).

The board of directors 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 uncertificated securities rules and the relevant 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 referred to above were passed by ordinary resolution on May 13, 2019 and remain in force as of the date of this Annual Report on Form 10-K.

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 and remain in force as of the date of this Annual Report on Form 10-K.

Alteration of Share Capital

In accordance with the Companies Act, the company may, by ordinary resolution, consolidate all or any of its share capital into shares of a larger nominal value than its existing shares, or sub-divide its shares, or any of them, into shares of a smaller amount than the existing shares.

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 and shall not be subject to any maximum.

Subject to the articles of association 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 our board of directors is 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, with eligibility for re-appointment at the end of such term. 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.

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 directors and unless otherwise fixed, it is two directors.

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 £1,000,000 per annum or such higher amount as may from time to time be decided by ordinary resolution. 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 losses and liabilities incurred by him in connection with the exercise of his or her duties or powers .

General Meetings

The company must convene and hold annual general meetings once a year 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 of association 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 not required for paying any preferential dividend (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

Neither U.K. law nor our articles of association 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" (e.g., the CREST System or DTC) 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 United Kingdom Laws and Regulations

Mandatory Bid

(i) The Takeover Code does not currently apply to the company. However if the company were to become subject to the Takeover Code in the future, the following provisions will apply. 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.
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,	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,

	England and Wales	Delaware
	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.	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.
Issue of New Shares	Under the Companies Act, the directors of a company must not	Under Delaware law, if the company's certificate of

	England and Wales	Delaware
	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.	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,	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

	England and Wales	Delaware
	in each case in accordance with the provisions of the Companies Act.	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.
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 (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.
Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each

	England and Wales	Delaware
	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.	stockholder is entitled to one vote for each share of capital stock held by such stockholder.
Shareholder Vote on Certain Transactions	The Companies Act provides for schemes of arrangement, which	Generally, under Delaware law, unless the certificate of

	England and Wales	Delaware
	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.	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.
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	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

	England and Wales	Delaware
	• to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	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.
Shareholder Litigation	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	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

England and Wales	Delaware
company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.	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.

U.K. Taxation Impacts on U.S. Holders of our Ordinary Shares

The discussion below 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 filing (both of which are subject to change at any time, possibly with retrospective effect) which related to our ordinary shares. 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 ordinary shares. In particular it should be noted that special rules may apply to certain persons such as market makers, brokers, dealers or intermediaries.

Dividends

Withholding Tax

Dividends paid by the company are not subject to any withholding or deduction for or on account of U.K. tax.

Stamp Duty and Stamp Duty Reserve Tax

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.

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

Citibank, N.A. acts 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 have appointed Citibank as depositary bank pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a Registration Statement on Form F-6 that was declared effective on May 23, 2019. 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 association, 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 association 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.

U.K. Taxation Impacts on U.S. Holders of our ADSs

The discussion below 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 filing (both of which are subject to change at any time, possibly with retrospective effect) which relate to our 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 our ADSs.

Stamp Duty and Stamp Duty Reserve Tax

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.

Bicycle Therapeutics Plc Share Option Plan

Form of Option Certificate

OPTION CERTIFICATE

THIS DEED is dated [□] 2019

THIS DEED is made between:

(1) **BICYCLE THERAPEUTICS PLC** registered in England with company number 11036004 whose registered office address is Building 900, Babraham Research Campus, Babraham, Cambridgeshire, CB22 3AT (the "**Company**"); and

(2) [*name of Optionholder*] of [*address of Optionholder*] (the "**Optionholder**").

BACKGROUND

(A) The Company has adopted the Bicycle Therapeutics Share Option Plan (the "**Plan**") which is governed by the rules set out in the Plan as amended from time to time (the "**Plan Rules**" and "**Rule**" shall be construed accordingly).

(B) The Company wishes to grant an option under the Plan to the Optionholder on the terms specified in this Deed (the "**Option Certificate**").

(C) The Optionholder is an [Employee/Consultant] of a Group Company (as "**Group Company**" is defined in the Plan Rules).

(D) [FOR INCENTIVE STOCK OPTIONS ONLY: Status of the Option. This Option is intended to qualify as an "incentive stock option" under Section 422 of the U.S. Internal Revenue Code of 1986, as amended (the "**Code**"), but the Company does not represent or warrant that this Option qualifies as such. The Optionholder should consult with his or her own tax advisors regarding the tax effects of this Option and the requirements necessary to obtain favorable income tax treatment under Section 422 of the Code, including, but not limited to, holding period requirements. To the extent any portion of this Option does not so qualify as an "incentive stock option," such portion shall be deemed to be a non-qualified stock option. If the Optionholder intends to dispose or does dispose (whether by sale, gift, transfer or otherwise) of any Shares within the one-year period beginning on the date after the transfer of such shares to him or her, or within the two-year period beginning on the day after the grant of this Option, he or she will so notify the Company within 30 days after such disposition.]

AGREED TERMS

1 INTERPRETATION

1.1 Terms defined in the Plan (but not defined in this Option Certificate) shall have the same meaning in this Option Certificate as in the Plan, unless the context requires otherwise. The rules of interpretation in the Plan also apply to the Option Certificate.

1.2 A copy of the Plan may be obtained on request.

1.3 Terms in the Option Certificate such as "**you**" and "**your**" refer to and address you in your capacity as the Optionholder.

2 GRANT OF OPTION

2.1 Subject to the other terms of this Option Certificate and the Plan, the Company grants you an option (the "**Option**") to acquire [□] ordinary shares (the "**Option Shares**") in the Company.

2.2 The Date of Grant of the Option is [□].

2.3 The Exercise Price of the Option is $[□] for each Option Share.

2.4 Subject to the Plan Rules, the Option shall normally Vest as follows:

[in equal tranches of 1/36th at the end of each calendar month following the Date of Grant.]

[in full on the Date of Grant.]

[as to ¼ of the total number of Shares under Option on the first anniversary of the Date of Grant and in respect of the remaining number of Shares under Option in equal tranches of 1/36th at the end of each calendar month following the first anniversary of the Date of Grant.]

3 EXERCISE OF OPTION

3.1 You may lose the ability to exercise the Option or the Option may lapse before it vests in accordance with clause 2.4 above if certain events occur, in accordance with the Plan Rules.

3.2 If you give or receive notice of termination of your employment or engagement with any Group Company you may not exercise your Option at any time while the notice remains effective.

3.3 To exercise the Option, you should complete and submit an exercise notice in the form and manner notified to you by the Company (which may be through an online share plan portal) and make payment (or other arrangements to the satisfaction of the Compensation Committee) of the aggregate Exercise Price and any liability to Tax ("**Tax Liability**") due.

4 LAPSE OF THE OPTION

4.1 Other than where your Option is transferred or assigned to your personal representatives or beneficiary in the event of your death, Options may not be transferred, assigned, pledged or charged and any purported transfer, assignment, pledge or charge shall cause the Option to lapse immediately.

4.2 The Option will lapse on the first to occur of:

(a) any transfer or purported transfer of the Option as described in clause 4.1 above;

(b) you making or attempting to make the Option subject to a charge or any other security interest;

(c) except as otherwise provided by the Plan Rules or determined by the Compensation Committee in accordance with the Plan Rules, the Cessation Date;

(d) the date on which you are declared bankrupt;

(e) the tenth anniversary of the Date of Grant; and

(f) any other date specified in the Plan Rules.

5 **TERMS OF OPTION**

5.1 The Option is subject to the Plan Rules (which are incorporated by reference in the Option Certificate), including Rule 6.4(h).

5.2 The Plan Rules shall take precedence over any conflicting statement about the terms of this Option Certificate.

6 **TAX LIABILITY**

By accepting the Option, you irrevocably agree to:

(a) pay to the Company, your employer or former employer (as appropriate) the amount of any Tax Liability; or

(b) enter into arrangements to the satisfaction of the Company, your employer or former employer (as appropriate) for payment of any Tax Liability.

7 **OPTIONHOLDER DECLARATION**

By countersigning this Option Certificate, you agree to be bound by the terms of this Option Certificate, the Plan Rules and any Group Company policy that may be applicable to you and the Option from time to time (the "**Policies**"). You have reviewed the Plan, this Option Certificate and the Policies in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Option Certificate and fully understand all provisions of the Plan Rules, this Option Certificate and the Policies. Save as otherwise provided in the Plan Rules, you hereby agree to accept as binding, conclusive and final all decisions or interpretations of the Compensation Committee upon any questions arising under the Plan or this Option Certificate.

This document has been executed as a deed and is delivered and takes effect on the date stated at the beginning of it.

DATED 26 September 2019

BicycleTX Ltd

and

Dr Michael Skynner

SERVICE AGREEMENT

THIS AGREEMENT is made on 26 September 2019

BETWEEN:

(1) **BICYCLETX LIMITED** a company incorporated under the laws of England and Wales (Company Number 11036101) whose registered office is at Building 900 Babraham Research Campus, Babraham, Cambridgeshire, CB22 3AT, United Kingdom (the "Company"); and

(2) **Dr MICHAEL SKYNNER** of (the ''Employee").

IT IS AGREED as follows:

1. COMMENCEMENT OF EMPLOYMENT

1.1 Your employment commenced on 1 January 2016 and shall continue unless and until either party gives notice to the other in accordance with paragraph 11 below. No employment with a previous employer is deemed to be continuous with your employment with the Company.

1.2 This Agreement shall take effect on the date first written above and replaces all and any previous employment agreements between you and the Company including (without limitation) the letter dated 23 November 2015 setting out your terms and conditions of employment (as amended on 2 February 2018) and your statement of main terms and conditions of employment dated 15 May 2019.

1.3 You warrant that by entering into this Agreement or any other arrangements with the Company you will not be in breach of or subject to any express or implied terms of any contract with, or other obligation to, any third party binding on you, including, without limitation, any notice period or the provisions of any restrictive covenants or confidentiality obligations arising out of any employment with any other employer or former employer.

1.4 You warrant that you have the right to work in the United Kingdom and you agree to provide to the Company copies of all relevant documents in this respect at the request of the Company. If at any time during the course of this Agreement you cease to have the right to work in the United Kingdom the Company may immediately terminate your employment without payment of compensation.

2. JOB TITLE

2.1 You shall serve as Chief Operating Officer ("COO") reporting to the CEO. The nature of the Company's business may result in changes occurring to the content of your role from time to time. You may also be required to carry out such additional or alternative tasks as may from time to time be reasonably required of you consistent with your executive level and job title, provided that these do not fundamentally change or undermine your position.

2.2 You shall faithfully and diligently perform such duties as you are required to undertake from time to time and exclusively devote the whole of your working time, skills, ability and attention to the business of the Company and use your best endeavours to promote the interests and reputation of the Company and (where applicable) any Group Company.

2.3 The Company may require you to carry out work for, or become a director or officer of, any Group Company at any time.

3. PLACE OF WORK

The Company's offices at Building 900, Babraham Research Campus, Babraham, Cambridge, UK or such other location as the Company may reasonably determine. The COO position may

require extensive international travel on business.

4. REMUNERATION

4.1 Your salary will be USD420,000 per annum paid monthly in arrears on or about the last working day of each month (less statutory and voluntary deductions) ("Salary"). Salary will be converted to GBP and paid in GBP based on the USD/GBP Bank of England daily spot exchange rate applicable on the date of this Agreement, with the exchange rate being revised according to the prevailing Bank of England daily spot exchange rate applicable on 1 January of each year. Your Salary will be reviewed annually in accordance with the Company's practices from time to time (which is expected to be by the end of the first quarter of each year). You will be notified in writing of any changes to your Salary or benefits.

4.2 You agree that the Company may deduct from the Salary or any other sum due to you (including any pay in lieu of notice) any amounts due to the Company including, without limitation, any overpayment of salary, loan or advance.

4.3 For the purposes of this Agreement your earned salary shall mean the proportion of your Salary earned by and due to you in each calendar year of employment with the Company ("Earned Salary").

4.4 **Annual Performance Bonuses:**

You will be eligible to participate in the Company's discretionary annual performance related bonus scheme to a maximum value of 40% of your Earned Salary in relation to your performance against agreed annual corporate and personal performance objectives as set out below (the "Annual Performance Bonus"). That is, if the compensation committee (the "Compensation Committee") of the board of directors ("the Board") of the Company's parent company, Bicycle Therapeutics plc ("BTL") determines that you have completed all such corporate and personal objectives to its satisfaction in a given year, your bonus would be 40% of your Earned Salary in that year, excluding any other bonuses in this offer. Such bonus may be payable in cash or, in whole or in part, in share options in BTL, as agreed by you and the Compensation Committee following notification by you of your preference at least 90 days prior to the normal payment date (and in the case of share options with the appropriate HMRC valuation process (if required by the Compensation Committee) and Board approval so as to be compliant with BTL's share option plan rules), with due consideration for the operational requirements of the Company at that time in your role as COO.

Any Annual Performance Bonus paid will not be pensionable and are subject to statutory applicable tax and National Insurance deductions. Performance will be assessed by the Compensation Committee at the end of each calendar year, against annual corporate and personal performance objectives agreed between you and the Board at the start of each calendar year, with any such bonus being payable in the first quarter of the following year. Qualification for your Annual Performance Bonus will require that you are employed by the Company (and have not served notice of termination of your employment to the Company) on 31 December of the year to which your bonus entitlement applies.

5 BENEFITS

5.1 The Company currently operates a personal pension plan provided by Scottish Widows Group. The Company will pay a sum equivalent to 12% of your basic annual earned salary into a personal pension plan selected by the Company. You may make additional contributions if you wish, but this is not mandatory. In the event that you elect, of your own volition, to opt-out of the Company's pension scheme then the Company will pay you in equal monthly instalments in arrears (less statutory deductions) a sum equivalent to the contribution that it would have

made into your pension scheme (the "Cash Equivalent Payment") less the Employer's National Insurance Contribution cost incurred by the Company as a result of making the Cash Equivalent Payment.

5.2 The Company currently operates a private healthcare scheme and subject to acceptance by the insurer on reasonable terms, you will be entitled to join.

5.3 The Company operates a death in service scheme which you automatically join upon commencement of employment.

5.4 Further details regarding benefits will be provided upon commencement of your employment. The Company reserves the right to replace or supplement any or all of the scheme(s) referred to in this paragraph 5, or to amend them at any time without compensation, provided that equivalent scheme(s) providing a similar level of benefit are put in place.

6 EXPENSES

The Company shall reimburse all reasonable out of pocket expenses properly incurred by you in the performance of the duties under this Agreement including travelling, subsistence and entertainment expenses provided you follow the Company's guidelines/allowances in force at the relevant time and provided that you shall, where reasonably practicable, provide the Company with vouchers, invoices or such other evidence of such expenses as the Company may reasonably require.

7 HOURS OF WORK

7.1 Your normal working hours are Monday to Friday from 9.00 am to 5.30 pm on each working day with one hour for lunch. You will be required to work such other hours as shall be reasonably necessary for you to perform your duties for which no further remuneration is payable.

7.2 By entering into this Agreement you confirm, that in your capacity as Chief Operating Officer you may choose or determine the duration of your working time and the working time limits set out in part II of the Working Time Regulations 1998 do not apply to you.

8 HOLIDAYS

8.1 In addition to the usual public holidays you will be entitled to 25 working days paid holiday in each calendar year. The holiday will accrue on a pro rata basis throughout each calendar year.

8.2 Holidays may only be taken at such time or times as are approved beforehand by the CEO, such approval not to be unreasonably withheld or delayed. You must give reasonable notice of proposed holiday dates by e-mailing the CEO or delegated director in advance, for approval.

8.3 The holiday year runs from January to December. With the agreement of the CEO, you may carry forward up to 5 days of untaken holiday into the next holiday year. Any carried over holiday must be taken by the end of March of the following calendar year or will be forfeited and no payment will be made in respect of any days so forfeited. You will not generally be permitted to take more than 10 days holiday at any one time.

8.4 Upon termination of your employment you will receive pay in lieu of accrued but untaken holiday. The Company may deduct an appropriate sum in respect of days taken in excess of your pro rata entitlement from your final remuneration on the basis that one day's holiday will be calculated as 1/260ths of your basic annual salary.

8.5 In the event that notice of termination of this Agreement is served by either party, the Company may require you to take any outstanding holiday during this notice period.

9 SICKNESS AND OTHER ABSENCE

9.1 If you are unable to attend at work by reason of sickness or injury or any unauthorised reason you must inform the Company as soon as possible on the first day of absence (and in any event not later than 11.00 am on the first day of absence) and, in the case of absence of uncertain duration, you must keep the Company regularly informed of your continued absence and your likely date of return. You are expected to observe this rule very strictly since failure to do so will entitle the Company to stop payment in respect of each day you fail to notify the Company.

9.2 If your absence, due to sickness or injury, is for less than seven (7) days, on your return to work you are required to immediately complete a self-certification form available from the Company. If your absence continues for more than seven (7) consecutive days (whether or not working days) you must provide the Company with a doctor's certificate from the seventh consecutive day of sickness or injury. This doctor's certificate must be provided to the Company promptly following the seventh consecutive day of absence. If illness continues after the expiry of the first certificate, further certificates must be provided promptly to cover the whole period of absence.

9.3 Subject to your compliance with the Company's sickness absence procedures (as amended from time to time), the Company may in its sole and absolute discretion pay full salary and contractual benefits during any period of absence due to sickness or injury for up to an aggregate of 3 months in any fifty-two (52) week period (whether such absence is continuous or intermittent in any calendar year). Such payment shall be inclusive of any statutory sick pay due in accordance with applicable legislation in force at the time of absence. The Company may, in its sole and absolute discretion, extend the period of allowance in an individual case if the circumstances so justify. Thereafter, the Company shall pay statutory sick pay or equivalent benefit to which you may be entitled subject to your compliance with the appropriate rules.

9.4 Whether absent from work or not, you may be, but only on reasonable grounds, required to undergo a medical examination by a Company doctor and your consent will be sought for a report to be sent to the Company.

9.5 The payment of sick pay in accordance with this paragraph 9 is without prejudice to the Company's right to terminate this Agreement prior to the expiry of your right to payments.

9.6 In the event you are incapable of performing your duties by reason of injuries sustained wholly or partly as a result of a third party's actions all payments made to you by the Company as salary or sick pay shall to the extent that compensation is recoverable from that third party constitute loans to you and shall be due and owing when and to the extent that you recover compensation for loss of earnings from the third party.

10 GARDEN LEAVE

10.1 After notice of termination has been given by you or the Company, the Company may at its discretion require you, for all or part of your notice period, to comply with any or all of the following instructions:

(a) not to carry out any further work for the Company or for any Group Company;

(b) to remain away from the Company's business premises and those of any Group Company (unless given written permission to do otherwise);

(c) not to contact any of the Company's clients, suppliers or employees or those of any Group Company without the Company's prior written permission;

(d) to carry out only part of your duties, or to carry out alternative duties or special projects for the Company within your skill set;

(e) to co-operate in the handover of your duties and responsibilities;

(f) to resign from any offices (including as a director) you hold within the Company or any Group Company or by virtue of your employment with us;

(g) to answer, in an honest and helpful way, such questions as the Company may reasonably ask of you;

(h) to keep the Company informed of your whereabouts and contact details and to remain reasonably contactable and available for work.

10.2 During any such period as described in paragraph 10.1 ("Garden Leave") the Company may appoint another person to carry out some or all of your duties. You will continue to owe all other duties and obligations (whether express or implied including fidelity and good faith) during Garden Leave and you shall continue to receive full pay and benefits (except that you will not accrue any further entitlement to any cash or equity incentive awards or bonus payments in respect of the Garden Leave period).

10.3 By placing you on Garden Leave, the Company will not be in breach of this Agreement or any implied duty of any kind whatsoever nor will you have any claim against the Company in respect of any such action.

10.4 During any period of Garden Leave you will remain readily contactable and available for work save when on paid holiday taken in accordance with paragraph 8. In the event that you are not available for work having been requested by the Company to do so, you will, notwithstanding any other provision of this Agreement, forfeit any right to salary and contractual benefits.

10.5 During any period of Garden Leave the Company may require you to deliver up any Confidential Information or property of the Company or any Group Company and upon instruction, delete any emails, spreadsheets or other Confidential Information and you will confirm your compliance with this paragraph 10.5 in writing if requested to do so by the Company.

10.6 During any period of Garden Leave the Company may require you to take any outstanding holiday entitlement.

11 NOTICE

11.1 Without prejudice to the Company's right to summarily terminate your employment in accordance with paragraph 11.3 below and your right to summarily terminate your employment for Good Reason in accordance with paragraph 11.4 below, either you or the Company may terminate your employment by giving to the other not less than six months' notice in writing.

11.2 The Company reserves the right in its sole and absolute discretion to give written notice to terminate your employment forthwith and to make a payment to you in lieu of salary and the benefits set out in paragraph 5 of this Agreement for all or any unexpired part of the notice period. For the avoidance of doubt, any payment in lieu made pursuant to this paragraph 11.2 will not include any element in relation to any payment in respect of (i) any Annual Performance Bonus or (ii) any holiday entitlement that would have otherwise accrued during the period for which the payment in lieu is made. For the further avoidance of doubt, if the Company elects to make a Payment in Lieu after notice of termination has been given by you, this will not constitute a termination by the Company without Cause for the purposes of paragraphs 11.7 and 11.8 below.

11.3 The Company may summarily terminate your employment hereunder (without notice) for Cause. For purposes of this Agreement, "Cause" shall mean where you:

(a) commit gross misconduct which includes, but is not limited to, dishonesty, fraud, theft, being under the influence of alcohol or drugs at work, causing actual or threatening

physical harm and causing damage to Company property;

(b) commit a material breach or non-observance of your duties or any of the provisions of this Agreement, or materially fail to observe the lawful directions of the Company, or breach any material Company policy or code of conduct, including but not limited to the Company's policy from time to time on matters relating to harassment;

(c) are convicted of a criminal offence (other than an offence under the road traffic legislation in the United Kingdom or elsewhere for which a non-custodial sentence is imposed);

(d) act in a manner which in the reasonable opinion of the Company, brings the Company into disrepute or otherwise prejudices or is in the reasonable opinion of the Company considered likely to prejudice the reputation of the Company;

(e) in the reasonable opinion of the Company, are guilty of any serious negligence in connection with or affecting the business or affairs of the Company;

(f) are unfit to carry out the duties hereunder because of sickness, injury or otherwise for an aggregate period of 26 weeks in any fifty-two (52) week period even if, as a result of such termination, you would or might forfeit any entitlement to benefit from sick pay under paragraph 9.3 above.

Any delay or forbearance by the Company in exercising any right of termination in accordance with this paragraph 11.3 will not constitute a waiver of such right.

11.4 You may summarily terminate your employment hereunder at any time (without notice) for Good Reason after complying with the Good Reason Process. For purposes of this Agreement, "Good Reason" shall mean that you have complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in your responsibilities, authority or duties; (ii) a material diminution in your Salary; (iii) a material change in the geographic location at which you provides services to the Company; or (iv) the material breach of this Agreement by the Company. "Good Reason Process" shall mean that (i) you reasonably determine in good faith that a "Good Reason" condition has occurred; (ii) you notify the Company in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) you cooperate in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) you terminate your employment (without notice) within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

11.5 Your employment hereunder shall also terminate immediately upon your death.

11.6 If your employment with the Company is terminated for any reason, the Company shall pay or provide to you (or to your authorised representative or estate) (i) any Salary earned through the Termination Date (as defined below); (ii) unpaid expense reimbursements (subject to, and in accordance with, paragraph 6 of this Agreement); and (iii) any vested benefits you may have under any employee benefit plan of the Company through the Termination Date, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (collectively, the "Accrued Benefits").

Severance Pay and Benefits Upon Termination by the Company without Cause or by the Executive for Good Reason outside the Change in Control Period.

11.7 If your employment is terminated on account of your death or by the Company without Cause (being for any reason not covered by paragraph 11.3), or you terminate your employment for

Good Reason (as provided in paragraph 11.4), in either case outside of the Change in Control Period, then the Company shall pay you the Accrued Benefits. In addition, subject to (i) your (or your authorised representative or estate signing, if the termination is due to your death) signing a settlement agreement and a separation agreement and release (together the "Settlement Agreements") in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities, a reaffirmation of all of your continuing obligations to the Company, including those set forth in paragraphs 13 – 15, and (in the case of the separation agreement and release) and a seven (7) business day revocation period; and (ii) the separation agreement and release becoming irrevocable, all within 60 days after the Termination Date (or such shorter period as set forth in the Settlement Agreements), the Company shall: (A) pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to nine (9) months of your salary as of the Termination Date (which payment shall not be reduced by either the value of any salary paid to you during your notice period or by any payment in lieu of notice made pursuant to paragraph 11.2); and (B) pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the cost to the Company of providing you with the contractual benefits under paragraph 5 for nine (9) months or, at the Company's option, continue to provide you with such benefits for nine (9) months.

Severance Pay and Benefits Upon Termination by the Company without Cause or by the Executive for Good Reason Within the Change in Control Period

11.8 The provisions of this paragraph 11.8 shall apply in lieu of, and expressly supersede, the provisions of paragraph 11.7 regarding severance pay and benefits upon a termination by the Company without Cause or by you for Good Reason if such termination of employment occurs within 12 months after the occurrence of the first event constituting a Change in Control (such period, the "Change in Control Period"). These provisions shall terminate and be of no further force or effect after the Change in Control Period.

(a) Change in Control Period. If during the Change in Control Period your employment is terminated on account of your death or by the Company without Cause (being for any reason not covered by paragraph 11.3) or you terminate your employment for Good Reason (as provided in paragraph 11.4), then, subject to (i) your signing (or your authorised representative or estate signing, if the termination is due to your death) a settlement agreement and a separation agreement and release (together the Settlement Agreements) in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities, a reaffirmation of all of your continuing obligations to the Company, including those set forth in paragraphs 13 – 15, and (in the case of the separation agreement and release) and a seven (7) business day revocation period; and (ii) the separation agreement and release becoming irrevocable, all within 60 days after the Termination Date (or such shorter period as set forth in the Settlement Agreements):

(i) the Company shall pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the sum of (A) your annual salary as of the Termination Date (or your annual salary in effect immediately prior to the Change in Control, if higher) plus (B) your target annual performance bonus amount under the Annual Bonus Plan for the then-current year (the "Change in Control Payment"), which payment shall not be reduced by either the value of any salary paid to you during your notice period or by the value of any payment made to you in lieu of notice pursuant to paragraph 11.2;

(ii) the Company shall: pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the cost to the Company of providing you with the contractual benefits under paragraph 5 for twelve (12) months or, at the Company's option, continue to provide you with such benefits for twelve (12) months; and

(iii) notwithstanding anything to the contrary in any applicable option agreement or other stock-based award agreement, all Time-Based Equity Awards shall immediately accelerate and become fully exercisable (for a period determined in accordance with the rules of the applicable equity plan) or nonforfeitable as of the later of (A) the Termination Date or (B) the Accelerated Vesting Date; *provided* that any termination or forfeiture of the unvested portion of such Time-Based Equity Awards that would otherwise occur on the Termination Date in the absence of this Agreement will be delayed until the Effective Date of the Settlement Agreements and will only occur if the vesting pursuant to this subsection does not occur due to the absence of the Settlement Agreements becoming fully effective within the time period set forth therein. Notwithstanding the foregoing, no additional vesting of the Time-Based Equity Awards shall occur during the period between your Termination Date and the Accelerated Vesting Date.

11.9 Definitions. For purposes of this paragraph 11, the following terms shall have the following meanings:

"Accelerated Vesting Date" means the effective date of the Settlement Agreements signed by you (or your authorised representatives or estate if the termination is due to your death).

"Termination Date" means the date on which your employment hereunder terminates.

"Time-Based Equity Awards" means all time-based stock options and other stock-based awards subject to time based vesting held by you.

"Change in Control" has the meaning given to that term in the Schedule to this Agreement.

12 DISCIPLINARY, DISMISSAL AND GRIEVANCE PROCEDURES

12.1 A copy of the Company's disciplinary, dismissal and grievance procedures are set out in its employee handbook (the "Employee Handbook").

12.2 Any grievance concerning your employment should be taken up orally in the first instance with the CEO. If the grievance is not resolved to your satisfaction, you should then refer it to the Chairman.

12.3 The Company reserves the right to suspend you on full pay and benefits at any time for a reasonable period to investigate any potential disciplinary matter that it reasonably believes you may be or may have been involved in.

13 OUTSIDE EMPLOYMENT, CONFIDENTIAL INFORMATION, CONFLICTING INTERESTS AND RETURN OF COMPANY PROPERTY

13.1 For the purposes of this paragraph 13, paragraph 10 above and paragraph 14 below the expression "Confidential Information" shall include, but not be limited to, any and all knowledge, data or information (whether or not recorded in documentary form or on computer disk or tape), which may be imparted in confidence or which is of a confidential nature or which you may reasonably regard as being confidential or a trade secret by the Company, concerning the

business, business performance or prospective business, financial information or arrangements, plans or internal affairs of the Company, any Group Company or any of their respective customers. By way of illustration but not limitation, "Confidential Information" includes (a) trade secrets, inventions, mask works, ideas, processes, formulas, software in source or object code, data, records, reports, interpretations, the contents of any databases, programs, other works of authorship, know-how, materials, improvements, discoveries, developments, technical information, designs and techniques and any other proprietary technology and all IPRs (as defined below) therein (collectively, "Inventions"); (b) information regarding research, development, new products, planned products, planned surveys, marketing surveys, research reports, market share and pricing statistics, marketing and selling, business plans, financial details, budgets and unpublished financial statements, licenses, prices and costs, fee levels, margins, discounts, credit terms, pricing and billing policies, quoting procedures, commissions, commission charges, other price sensitive information, methods of obtaining business and other business methods, forecasts, future plans and potential strategies, financial projections and business strategies and targets, operational plans, financing and capital-raising plans, activities and agreements, internal services and operational manuals, methods of conducting Company business, corporate and business accounts, suppliers and supplier information, and purchasing; (c) information regarding clients or customers and potential clients or customers of the Company, including customer lists, client lists, names, addresses (including email), telephone, facsimile or other contact numbers and contact names, representatives, their needs or desires with respect to the types of products or services offered by the Company, proposals, bids, contracts and their contents and parties, the type and quantity of products and services provided or sought to be provided to customers and potential customers of the Company and other non-public information relating to customers and potential customers; (d) information regarding any of the Company's business partners and their services, including names, representatives, proposals, bids, contracts and their contents and parties, the type and quantity of products and services received by the Company, and other non-public information relating to business partners; (e) information regarding personnel, computer passwords, employee lists, compensation and remuneration, and employee skills; and (f) any other non-public information which a competitor of the Company could use to the competitive disadvantage of the Company.

13.2 You shall not, without the prior written consent of the Company, either solely or jointly, directly or indirectly, carry on or be engaged, concerned or interested in any other trade or business, including, but not limited to, carrying on business with the Company's suppliers or dealers, save that nothing in this paragraph 13.2 shall prevent you from holding (with the prior written consent of the Company, which shall not be unreasonably delayed or withheld) up to three percent (3%) of the issued equity share capital of any company where those equity shares are listed on a recognised investment exchange (as defined in section 285 of the Financial Services and Markets Act 2000) or traded on the AIM market operated by the London Stock Exchange. Failure to secure advance permission in accordance with this paragraph 13.2 may result in summary dismissal.

13.3 You will not (except with the prior written consent of the Board) except in the proper course of your duties during the continuance of this Agreement (which for the avoidance of doubt shall include the use of laptops and remote working), or at any time thereafter:

(a) disclose or use for your own or for another's purpose or benefit any Confidential Information which you may learn while in the employment of the Company except as required by a court of law or any regulatory body or that which may be in or become part of the public domain other than through any act or default on your part;

(b) copy or reproduce in any form or by or on any media or device or allow others access to copy or reproduce any documents (including without limitation letters, facsimiles and

memoranda), disks, memory devices, notebooks, tapes or other medium whether or not eye-readable and copies thereof on which Confidential Information may from time to time be recorded or referred to ("Documents"); or

(c) remove or transmit from the Company or any Group Company's premises any Documents on which Confidential information may from time to time be recorded.

13.4 Upon termination of your employment for any reason by either party, you must immediately return to the Company all Company property including but not limited to documents, papers, records, keys, credit cards, mobile telephones, computer and related equipment, PDA or similar device, security passes, accounts, specifications, drawings, lists, correspondence, catalogues or the like relating to the Company's business which is in your possession or under your control and you must not take copies of the same without the Company's express written authority.

14 RESTRICTIVE COVENANTS

14.1 For the purpose of this paragraph 14 the following expressions shall have the following meanings:

"Prospective Customer" shall mean any person, firm, company or other business who was to your knowledge at the Termination Date negotiating with the Company or with any Group Company with a view to dealing with the Company or any Group Company as a customer;

"Restricted Business" means any business which (i) carries on research in the field of constrained peptides, including, without limitation, all work in the field of lead constrained peptide identification and optimization and pre-clinical development of constrained peptide therapeutics or (ii) is developing a drug conjugate compound for treating cancer that targets the same target as a drug conjugate compound in development by any Group Company;

"Restricted Customers" shall mean any person, firm, company or other business who was to your knowledge at any time in the twelve (12) month period ending with the Termination Date a customer of the Company or any Group Company;

"Restricted Period" shall mean the period of twelve (12) months from the Termination Date;

"Restricted Territory" means anywhere in the United States or the United Kingdom or in any other country in which the Company or any Group Company conducts business or as of the date of termination of my employment relationship had plans to conduct business; and

"Termination Date" shall mean the date on which your employment under this Agreement terminates either due to you or the Company terminating it in accordance with the terms of the Agreement or in breach of the terms of this Agreement.

14.2 During the course of your employment hereunder you are likely to obtain Confidential Information relating to the business of the Company or any Group Company and personal knowledge and influence over clients, customers and employees of the Company or any Group Company. You hereby agree with the Company that to protect the Company's and any and all Group Company's business interests, customer connections and goodwill and the stability of its or their workforce, that you will not during the Restricted Period (and in respect of sub-paragraph 14.2(f) below only, at any time):

(a) in the Restricted Territory, compete with the business of the Company or any Group Company by being directly or indirectly employed or engaged in any capacity by any person, firm or company which engages in or provides Restricted Business or commercial activities competitive with the Restricted Business to Restricted Customers or Prospective Customers;

(b) in the Restricted Territory, compete with the business of the Company or any Group Company either on your own account or for any person, firm or company directly or indirectly by transacting business in competition with the Restricted Business with any Restricted Customer or Prospective Customer of the Company or Group Company and with whom you personally dealt in respect of Restricted Business in the pursuance of the employment hereunder in the twelve (12) months prior to the Termination Date;

(c) in the Restricted Territory, compete with the business of the Company or any Group Company either on your own account or for any person, firm or company directly or indirectly in competition with the Restricted Business by soliciting or endeavouring to solicit or entice the business or custom of any Restricted Customer or Prospective Customer and with whom you personally dealt in respect of Restricted Business in the pursuance of the employment hereunder in the twelve (12) months prior to the Termination Date;

(d) either on your own account or for any person, firm or company directly or indirectly solicit or entice away or endeavour to solicit or entice away any director or senior employee of the Company or any Group Company employed in a managerial, scientific or technical role with whom you have had material personal dealings in the twelve (12) months prior to the Termination Date;

(e) from the Termination Date for the purpose of carrying on any trade, or business represent or allow you to be represented or held out as having any present association with the Company or any Group Company; and

(f) from the Termination Date carry on any trade or business whose name incorporates the word Bicycle or any deviation or extension thereof which is likely or which may be confused with the name of the Company or any Group Company.

14.3 While the restrictions set out in paragraph 14.2 above are considered by the parties to be reasonable in all the circumstances, it is agreed that if any one or more of such restrictions shall either taken by itself or themselves together be adjudged to go beyond what is reasonable in all the circumstances for the protection of the legitimate interests of the Company but would be adjudged reasonable if any particular restriction or restrictions were deleted or if any part or parts of the wording thereof were deleted, restricted or limited in a particular manner, then the restrictions set out in paragraph 14.2 above shall apply with such deletions or restrictions or limitations as the case may be.

14.4 For the avoidance of doubt nothing in this paragraph 14 shall prevent you from having any dealings with any Prospective Customer or Restricted Customer in relation to any business which is not Restricted Businesses and which is not competitive with the Restricted Business, nor from continuing to deal with any Prospective Customer or Restricted Customer where you either have a social or business relationship unconnected to the Company and that relationship does not compete with the Restricted Business.

14.5 The restrictions contained in paragraph 14.2 above are held by the Company for itself and on trust for any other Group Company and shall be enforceable by the Company on their behalf or by any Group Company (at their request). You shall during the employment hereunder enter into direct agreements with any Group Company whereby you will accept restrictions in the same or substantially the same form as those contained in paragraph 14.2 above.

14.6 In the event that the Company exercises its rights and places you on Garden Leave under paragraph 10 above then the Restricted Period shall be reduced by any period/s spent by you on Garden Leave prior to the Termination Date.

14.7 During the Restricted Period you shall provide a copy of the restrictions contained at paragraph 13 above and this paragraph 14 to any employer or prospective employer or any other party with whom you become or will become engaged or provide service or services to.

15 INTELLECTUAL PROPERTY

15.1 For the purpose of this paragraph 15 “IPRs" shall mean all trade secrets, Copyrights, trademarks and trade and business names (including goodwill associated with any trademark or trade or business names and the right to sue for passing off or unfair competition), service marks, mask work rights, patents, petty patents, rights in ideas, concepts, innovations, discoveries, developments and improvements, drug formulations, technology, rights in domain names, rights in inventions, utility models, rights in know-how (including all data, methods, processes, practices and other results of research), unregistered design rights, registered design rights, database rights, semiconductor topography rights and other intellectual property rights recognized by the laws of any jurisdiction or country including all applications and rights to apply for and be granted, renewals or extensions of, and rights to claim priority from, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world; the term “Copyright” means the exclusive legal right to reproduce, perform, display, distribute and make derivative works of a work of authorship (as a literary, musical, or artistic work) recognized by the laws of any jurisdiction or country; and the term “Moral Rights” means all paternity, integrity, disclosure, withdrawal, special and any other similar rights recognized by the laws of any jurisdiction or country.

15.2 It is contemplated that you may in the course of your employment with the Company create, author or originate (either alone or jointly with others) Inventions (as defined in paragraph 13.1), and/or records, reports, papers, databases, data, information, know how, literature, drawings, graphics, typographical arrangements, designs, works, documents, publications and other materials (in printed, electronic, or any other media or form) (together with Inventions constituting “Works”).

15.3 You will promptly disclose to the Company full details of any Inventions on their creation and provide further details, explanations and demonstrations as the Company from time to time requests.

15.4 All IPRs subsisting in any Works shall be the exclusive property of the Company.

15.5 To the extent that such IPRs do not vest automatically in the Company by operation of law, you hereby assign and agree to assign to the Company all of your right, title and interest in any existing and future IPRs which may subsist in any Works for their full term of protection (including any extensions, revivals and renewals) together with the right to sue and claim remedies for past infringement and all materials embodying these rights to the fullest extent permitted by law in any and all countries of the world. Insofar as such IPRs do not vest automatically by operation of law or under this Agreement, the Consultant holds legal title in these rights and inventions on trust for the Company.

15.6 To the extent permitted by law you hereby irrevocably and unconditionally waive in favour of the Company, its licensees and successors in title, all existing and future Moral Rights (or similar rights existing in any part of the world) you may have in respect of any Works under Chapter IV of the Copyright Designs and Patents Act 1988 in England or any similar provisions of law in any jurisdiction, including (but without limitation) the right to be identified, the right of integrity and the right against false attribution, and agrees not to institute, support, maintain or permit any action or claim to the effect that any treatment, exploitation or use of such Works, Inventions or other materials infringes the Consultant's Moral Rights.

15.7 Without prejudice to the generality of paragraph 15.9 below, during your employment with the

Company and thereafter, without limit in time, you shall at the request and expense of the Company, promptly assist the Company:

(a) to file, prosecute, obtain and maintain registrations and applications for registration of any IPRs subsisting in, or protecting, any Works; and

(b) to commence and prosecute legal and other proceedings against any third party for infringement of any IPRs subsisting in, or protecting, any Works and to defend any proceedings or claims made by any third party that the use or exploitation of any Works infringes the IPRs or rights of any third party.

15.8 You shall keep details of all Inventions confidential and shall not disclose the subject matter of any Inventions to any person outside the Company without the prior consent of the Company. You acknowledge that any unauthorised disclosure of such subject matter may prevent the Company from obtaining patent or registered intellectual property protection for such Invention.

15.9 Whenever requested to do so by the Company and in any event on the termination or expiry of this Agreement, you shall promptly deliver to the Company all correspondence, documents, papers and records on all media (and all copies or abstracts of them), recording or relating to any part of the Works and the process of their creation which are in your possession, custody or power.

15.10 Subject to paragraph 15.11 below, during your employment with the Company and thereafter without limit in time you shall at the request and expense of the Company promptly execute and do all acts, matters, documents and things necessary or desirable to give the Company the full benefit of the provision of this paragraph 15. You shall not register nor attempt to register any of the IPRs in the Works, nor any of the Inventions, unless requested to do so in writing by the Company.

15.11 Nothing in this paragraph 15 shall be construed, or have the effect of, restricting your rights under sections 39 to 43 (inclusive) of the Patents Act 1977 (as amended from time to time).

16 LITIGATION ASSISTANCE

During the term of your employment and at all times thereafter subject always to your obligations to third parties, you shall furnish such information and proper assistance to the Company or any Group Companies as it or they may reasonably require in connection with the Company's intellectual property (including without limitation applying for, defending, maintaining and protecting such intellectual property) and in connection with litigation in which it is or they are or may become a party. This obligation on you shall include, without limitation, meeting with the Company or any Group Companies' legal advisers, providing witness evidence, both in written and oral form, and providing such other assistance that the Company or any Group Companies' legal advisors in their reasonable opinion determine. The Company shall reimburse you for all reasonable out of pocket expenses incurred by you in furnishing such information and assistance and in the event you are no longer employed by the Company a reasonable daily rate (as agreed between you and the Company for such assistance). Such assistance shall not require you to provide assistance for more than 5 days in any calendar month. For the avoidance of doubt the obligations under this paragraph 16 shall continue notwithstanding the termination of your employment with the Company.

17 COLLECTIVE AGREEMENTS

There are no collective agreements which directly affect your terms and conditions of employment.

18 DATA PROTECTION

Processing of personal data and our policies

18.1 Information relating to an individual (or from which an individual may be identified) is called "personal data".

18.2 In processing personal data, we are required to comply with the law on data protection. To help us achieve this, we have produced a privacy notice ("Privacy Notice"). This may be found in the Employee Handbook. You must read this and comply with it in carrying out your work.

Data protection principles

18.3 In complying with the law on data protection, we are required to comply with what are known as data protection principles. These are summarised in our Privacy Notice. In performing your role and carrying out your responsibilities, you must do your best to ensure that we comply with these principles.

18.4 A key element of the data protection principles is the duty to ensure that data is processed securely and protected against unauthorised or unlawful processing or loss. Key elements include the following:

You must ensure that laptops, memory sticks, phones and other mobile devices are password protected and encrypted. You must not take such devices outside the office without encryption. You must take care of them and keep them secure.

You must use strong passwords, changing them when asked and not sharing them with unauthorised colleagues.

You must not access other individuals' personal data unless in the course of your work.

Data breach – and urgent notification

18.5 If you discover a data breach, you **must** notify the Chairman or CFO immediately – and, if practicable, within one hour. Depending on context, you may then need to provide further information on the circumstances of the breach.

18.6 A data breach occurs where there is destruction, loss, alteration or unauthorised disclosure of or access to personal data which is being held, stored, transmitted or processed in any way. For example, there is a data breach if our servers are hacked or if you lose a laptop or USB stick or send an email to the wrong person by mistake.

18.7 Failure to notify a breach or to provide information as set out above will be treated seriously and disciplinary action may be taken.

Why we process personal data

18.8 For information on the nature of the data we process, why we process it, the legal basis for processing and related matters, please refer to our Privacy Notice. In summary:

(a) We process personal data relating to you for the purposes of our business including management, administrative, employment and legal purposes.

(b) We monitor our premises and the use of our communication facilities, including using CCTV cameras, monitoring compliance with our data and IT policies, and where non-compliance is suspected, looking in a more targeted way.

18.9 The summary above is for information only. We do not, in general, rely on your consent as a legal basis for processing. Agreeing the terms of this Agreement will not constitute your giving consent to our processing of your data.

18.10 We reserve the right to amend the documents referred to above from time to time.

19 THIRD PARTY RIGHTS

Save in respect of any rights conferred by this Agreement on any Group Company (which such

Group Company shall be entitled to enforce), a person who is not a party to this Agreement may not under the Contracts (Rights of Third Parties) Act 1999 enforce any of the terms contained within this Agreement.

20 DEFINITIONS

In this Agreement:

"Group Company" means a subsidiary or affiliate and any other company which is for the time being a holding company of the Company or another subsidiary or affiliate of any such holding company as defined by the Companies Act 2006 (as amended) and "Group Companies" will be interpreted accordingly.

21 ENTIRE AGREEMENT

These terms and conditions constitute the entire agreement between the parties and supersede any other agreement whether written or oral previously entered into.

22 JURISDICTION AND CHOICE OF LAW

This Agreement shall be governed by and interpreted in accordance with the laws of England and Wales and the parties to this Agreement submit to the exclusive jurisdiction of the Courts of England and Wales in relation to any claim, dispute or matter arising out of or relating to this Agreement.

23 NOTICES

Any notices with respect to this Agreement shall be in writing and shall be deemed given if delivered personally (upon receipt), sent by email or sent by first class post addressed, in the case of the Company, to the Company Secretary at its registered office and in your case, addressed to your address last known to the Company.

Schedule

Definitions

Change in Control: means and includes each of the following:

(a) a Sale; or

(b) a Takeover.

The Compensation Committee shall have full and final authority, which shall be exercised in its sole discretion, to determine conclusively whether a Change in Control has occurred pursuant to the above definition, the date of the occurrence of such Change in Control and any incidental matters relating thereto; provided that any such Change in Control also qualifies as a "change in control event" as defined in Section 409A of the United States Internal Revenue Code of 1986, as amended and the regulations and other guidance thereunder and any state law of similar effect, and any exercise of authority in conjunction with a determination of whether a Change in Control is a "change in control event" is consistent with such regulation.

Control: shall have the meaning given to that word by Section 719 of the UK Income Tax (Earnings and Pensions) Act 2003 and "**Controlled**" shall be construed accordingly.

Sale: the sale of all or substantially all of the assets of BTL.

Takeover: circumstances in which any person (or a group of persons acting in concert) (the "**Acquiring Person**"):

(a) obtains Control of BTL as the result of making a general offer to:-

i. acquire all of the issued ordinary share capital of BTL, which is made on a condition that, if it is satisfied, the Acquiring Person will have Control of BTL; or

ii. acquire all of the shares in BTL; or

(b) obtains Control of BTL as a result of a compromise or arrangement sanctioned by a court under Section 899 of the UK Companies Act 2006, or sanctioned under any other similar law of another jurisdiction; or

(c) becomes bound or entitled under Sections 979 to 985 of the UK Companies Act 2006 (or similar law of another jurisdiction) to acquire shares in BTL; or

(d) obtains Control of BTL in any other way, including but not limited to by way of a merger.

THIS AGREEMENT has been executed and delivered as a deed by or on behalf of the parties on the date written at the top of page 1.

Executed as a Deed by **BICYCLETX LIMITED** acting by a director:

/s/ Kevin Lee (Director)

in the presence of:

/s/ Paula Barnes

Witness Name: Paula Barnes

Witness Address:

Executed as a Deed by **MICHAEL SKYNNER**:

/s/ Michael Skynner (Michael Skynner)

in the presence of:

/s/ Gabriela Repeta

Witness Name: Gabriela Repeta

Witness Address:

Exhibit 10.10

AMENDED AND RESTATED EMPLOYMENT AGREEMENT

This **AMENDED AND RESTATED EMPLOYMENT AGREEMENT** (the "***Agreement***") is entered into effective as of September 26th, 2019 (the "***Effective Date***"), by and between Nicholas Keen ("***Executive***") and Bicycle Therapeutics Inc. (the "***Company***").

Executive has been employed by the Company as its Chief Scientific Officer pursuant to the Employment Agreement with the Company dated January 3, 2017, which was then amended and restated May 28, 2019 (collectively, the "***Prior Agreements***").

The Company desires to continue to employ Executive and, in connection therewith, to compensate Executive for Executive's personal services to the Company; and

Executive wishes to continue to be employed by the Company and provide personal services to the Company in return for certain compensation.

Accordingly, in consideration of the mutual promises and covenants contained herein, the parties agree to the following:

1. EMPLOYMENT BY THE COMPANY.

1.1 At-Will Employment. Executive shall continue to be employed by the Company on an "at-will" basis, meaning either the Company or Executive may terminate Executive's employment at any time, with or without Cause (as defined in Section 6.2(f) below), Good Reason (as defined in Section 6.2(e) below), or advance notice. Any contrary representations that may have been made to Executive shall be superseded by this Agreement. This Agreement shall constitute the full and complete agreement between Executive and the Company on the "at-will" nature of Executive's employment with the Company, which may be changed only in an express written agreement signed by Executive and a duly authorized officer of the Company. Executive's rights to any salary or cash bonus following a termination shall be only as set forth in Section 6 or under any applicable benefit or equity plan.

1.2 Position. Subject to the terms set forth herein, the Company agrees to continue to employ Executive and Executive hereby accepts such continued employment. In addition, Executive shall continue to serve as Chief Scientific Officer. During the term of Executive's employment with the Company, and excluding periods of vacation and sick leave to which Executive is entitled, Executive shall devote all business time and attention to the affairs of the Company necessary to discharge the responsibilities assigned hereunder, and shall use commercially reasonable efforts to perform faithfully and efficiently such responsibilities.

1.3 Duties. Executive will continue to render such business and professional services in the performance of Executive's duties (consistent with Executive's position as Chief Scientific Officer) to the Company, and for the benefit of the Company's parent, Bicycle Therapeutics plc ("***BTL***"). Executive shall continue to report to BTL's Chief Executive Officer. For the avoidance of doubt and for ease of understanding the intent of the arrangement, all of Executive's services described herein shall be provided directly to the Company, which will, in turn, continue to provide

such services to BTL pursuant to an arm's length intra-company agreement. To the extent that Executive engages in any services contemplated herein on BTL's behalf that involve the execution and negotiation of legal documents, such services will be performed in the United Kingdom. Executive shall continue to be expected to perform Executive's duties under this Agreement out of the Company's office in Lexington, Massachusetts, or such other location as assigned. In addition, Executive shall make such business trips to such places as may be reasonably necessary or advisable for the efficient operations of the Company.

1.4 Company Policies and Benefits. The employment relationship between the parties shall continue to be subject to the Company's written personnel policies and procedures as they may be adopted, revised, or deleted from time to time in the Company's sole discretion. Executive will continue to be eligible to participate on the same basis as similarly-situated employees in the Company's benefit plans in effect from time to time during Executive's employment. Subject to the preceding sentence, the Company reserves the right to change, alter, or terminate any benefit plan in its sole discretion. All matters of eligibility for coverage or benefits under any benefit plan shall be determined in accordance with the provisions of such plan. Notwithstanding the foregoing, in the event that the terms of this Agreement differ from or are in conflict with the Company's general employment policies or practices, this Agreement shall control.

1.5 Vacation. During the term of Executive's employment with the Company, Executive shall continue to accrue five weeks of paid time off per calendar year (prorated for partial years), subject to the Company's paid time off policy, as in effect from time to time.

1.6 Pension. During the term of Executive's employment with the Company, Executive shall continue to be eligible to receive up to four (4) percent of Base Salary as contributions to a safe harbor 401(k) plan.

2. COMPENSATION.

2.1 Salary. Executive shall receive an annualized base salary of $380,000, subject to review and increase (but not decrease) from time to time by the Company in its sole discretion, payable subject to standard federal and state payroll withholding requirements in accordance with the Company's standard payroll practices (the "***Base Salary***").

2.2 Bonus.

(a) During Employment. Executive shall be eligible to earn an annual performance bonus (the "***Annual Bonus***") with an annual target of 35% (the "***Target Percentage***") of Executive's then-current Base Salary. The Annual Bonus will be based upon the assessment by the Board of Directors of the Company (the "***Board***") or a committee thereof of Executive's performance and the Company's attainment of targeted goals (as set by the Company and confirmed by the Board in its reasonable good faith discretion) over the applicable calendar year. The Annual Bonus, if any, will be subject to applicable payroll deductions and withholdings. No amount of any Annual Bonus is guaranteed at any time, and, except as otherwise stated in Sections 6.3(a)(iii), Executive must be an employee in good standing through the date the Annual Bonus is paid to be eligible to receive an Annual Bonus, except as set forth in Section 6.1(a). No partial or prorated bonuses will be provided. Subject to Section 6.3(b) related to payments upon certain terminations of

employment, any Annual Bonus, if earned, will be paid at the same time annual bonuses are generally paid to other similarly-situated employees of the Company. Executive's eligibility for an Annual Bonus is subject to change in the discretion of the Board (or any authorized committee thereof).

(b) Upon Termination. Subject to the provisions of Section 6, in the event Executive leaves the employ of the Company for any reason prior to the date the Annual Bonus is paid, Executive is not eligible to earn such Annual Bonus, prorated or otherwise.

(c) Equity Awards. The equity awards held by the Executive shall continue to be governed by the terms and conditions of the Company's applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such equity awards held by the Executive (collectively, the "Equity Documents"); provided, however, and notwithstanding anything to the contrary in the Equity Documents, Section 6.3(a)(iv) of this Agreement shall apply in the event of a termination by the Company without Cause or by the Executive for Good Reason, in either case within 12 months after a Change in Control (as defined in **Exhibit A** hereto).

2.3 Expense Reimbursement. The Company will reimburse Executive for reasonable business expenses in accordance with the Company's standard expense reimbursement policy, subject to any applicable payroll withholdings and deductions (if any). For the avoidance of doubt, to the extent that any reimbursements payable to Executive are subject to the provisions of Section 409A of the Internal Revenue Code of 1986, as amended (the "***Code***"): (a) any such reimbursements will be paid no later than December 31 of the year following the year in which the expense was incurred, (b) the amount of expenses reimbursed in one year will not affect the amount eligible for reimbursement in any subsequent year, and (c) the right to reimbursement under this Agreement will not be subject to liquidation or exchange for another benefit.

3. CONFIDENTIAL INFORMATION, INVENTIONS, NON-SOLICITATION AND NON-COMPETITION OBLIGATIONS. In connection with Executive's continued employment with the Company and in exchange for good and valuable consideration, Executive will continue to receive and continue to have access to the Company's confidential information and trade secrets. Accordingly, and in consideration of the benefits that Executive is eligible to receive under this Agreement, Executive agrees to sign the Company's Employee Confidential Information, Inventions, Non-Solicitation and Non-Competition Agreement (the "***Confidential Information Agreement***"), attached as **Exhibit B**, which contains restrictive covenants and prohibits unauthorized use or disclosure of the Company's confidential information and trade secrets, among other obligations. The Confidential Information Agreement contains provisions that are intended by the parties to survive and do survive termination or expiration of this Agreement and will supersede, prospectively only, the agreement that Executive previously signed relating to the same subject matter.

4. OUTSIDE ACTIVITIES. Except with the prior written consent of the Board, Executive will not, while employed by the Company, undertake or engage in any other employment, occupation, or business enterprise that would interfere with Executive's responsibilities and the performance of Executive's duties hereunder except for (i) reasonable time devoted to volunteer services for or on behalf of such religious, educational, non-profit, and/or other charitable organization as Executive may wish to serve, (ii) reasonable time devoted to activities in the non-profit and business communities consistent with Executive's position with the Company, (iii) reasonable time serving as trustee, director, or advisor to any family companies or trusts, (iv) with prior written notice to the

Board, reasonable time devoted to service as a member of the board of directors (or its equivalent in the case of a non-corporate entity) of a non-competing business, or (v) provide consulting services for up to 8 hours per month; so long as the activities set forth in clauses (i), (ii), (iii), (iv) and (v) (A) do not, individually or in the aggregate, interfere with the performance of the Executive's duties under this Agreement, (B) are not contrary to the interests of the Company or its Affiliates or competitive in any way with the Company its Affiliates or (C) are not in the field of constrained peptide drugs or therapeutics (including, without limitation, any work in the field of lead peptide identification and optimization and pre-clinical development of constrained peptide therapeutics). In addition, the activities set forth in clauses (i), (ii), (iii), and (iv) may not exceed, in the aggregate, 6 days of Executive's services per year, which permitted time commitment may be increased by the Board, in its discretion which shall not be unreasonably withheld, to up to 12 days per year where a new specific opportunity has been identified by Executive which would give Executive experience that is considered to be of wider benefit to the Company. This restriction shall not, however, preclude Executive from (x) owning less than one percent (1%) of the total outstanding shares of a publicly traded company, (y) managing Executive's passive personal investments, or (z) employment or service in any capacity with Affiliates of the Company. As used in this Agreement, "***Affiliates***" means, at the time of determination, any "parent" or "subsidiary" of the Company as such terms are defined in Rule 405 of the Securities Act of 1933, as amended. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

5. **NO CONFLICT WITH EXISTING OBLIGATIONS**. Executive represents that Executive's performance of all the terms of this Agreement and continued service as an employee of the Company do not and will not breach any agreement or obligation of any kind made prior to Executive's employment by the Company, including agreements or obligations Executive may have with prior employers or entities for which Executive has provided services. Executive has not entered into, and Executive agrees that Executive will not enter into, any agreement or obligation, either written or oral, in conflict herewith or with Executive's duties to the Company.

6. **TERMINATION OF EMPLOYMENT.** The parties acknowledge that Executive's employment relationship with the Company continues to be at-will. Either Executive or the Company may terminate the employment relationship at any time, with or without Cause (as defined below) or advance notice. The provisions in this Section govern the amount of compensation, if any, to be provided to Executive upon termination of employment and do not alter this at-will status.

6.1 **Termination by Virtue of Death or Disability of Executive**.

(a) In the event of Executive's death while employed pursuant to this Agreement, all obligations of the parties hereunder and Executive's employment shall terminate immediately, and the Company shall, pursuant to the Company's standard payroll policies and applicable law, pay to Executive's legal representatives the Accrued Obligations (as defined in Section 6.2(d) below) due to Executive, along with any Special Bonus Payment (as that term is defined below).

(b) Subject to applicable state and federal law, the Company shall at all times have the right, upon written notice to Executive, to terminate this Agreement based on

Executive's Disability (as defined below). Termination by the Company of Executive's employment based on "***Disability***" shall mean termination because Executive is unable due to a physical or mental condition to perform the essential functions of Executive's position with or without reasonable accommodation for six (6) months in the aggregate during any twelve (12) month period or based on the written certification by two licensed physicians of the likely continuation of such condition for such period. This definition shall be interpreted and applied consistent with the Americans with Disabilities Act, the Family and Medical Leave Act, and other applicable law. In the event Executive's employment is terminated based on Executive's Disability, Executive will be entitled to the Accrued Obligations due to Executive, along with any Special Bonus Payment (as that term is defined below).

(c) If the Executive's termination due to death or Disability occurs between January 1 and the payment date of the Annual Bonus that Executive would have otherwise earned for performance in the calendar year preceding the termination due to death or Disability, then and only then will Executive be paid the full Annual Bonus amount that Executive would have otherwise earned for performance in such preceding calendar year (the "***Special Bonus Payment***").

6.2 Termination by the Company or Resignation by Executive.

(a) The Company shall have the right to terminate Executive's employment pursuant to this Section 6.2 at any time (subject to any applicable cure period stated in Section 6.2(f)) with or without Cause or advance notice, by giving notice as described in Section 7.1 of this Agreement. Likewise, Executive can resign from employment with or without Good Reason, by giving notice as described in Section 7.1 of this Agreement. Executive hereby agrees to comply with the additional notice requirements set forth in Section 6.2(e) below for any resignation for Good Reason. If Executive is terminated by the Company (with or without Cause) or resigns from employment with the Company (with or without Good Reason), then Executive shall be entitled to the Accrued Obligations (as defined below). In addition, if Executive is terminated without Cause or resigns for Good Reason, and provided that such termination constitutes a "separation from service" (as defined under Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder, a "***Separation from Service***"), and further provided that Executive executes and allows to become effective a separation agreement that includes, among other terms, a general release of claims in favor of the Company and its Affiliates and representatives and a non-competition clause, in the form presented by the Company (the "***Separation Agreement***"), and subject to Section 6.2(b) (the date that the general release of claims in the Separation Agreement becomes effective and may no longer be revoked by Executive is referred to as the "***Release Date***"), then Executive shall be eligible to receive the following severance benefits (collectively the "***Non-CIC Severance Benefits***"):

(i) An amount equal to nine (9) months of Executive's then current Base Salary, less standard payroll deductions and withholdings, paid in installments on the Company's regular payroll dates; and

(ii) Provided Executive or Executive's covered dependents, as the case may be, timely elects continued coverage under COBRA under the Company's group health plans following such termination, the portion of the COBRA premiums which is equal to the cost of the coverage that the Company was paying as of the date of termination, to continue Executive's (and Executive's covered dependents, as applicable) health insurance

coverage in effect on the termination date until the earliest of: (1) nine (9) months following the termination date; (2) the date when Executive becomes eligible for substantially equivalent health insurance coverage in connection with new employment or self-employment; or (3) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination (such period from the termination date through the earlier of (1)-(3), (the "***COBRA Payment Period***")). Notwithstanding the foregoing, if at any time the Company determines that its payment of COBRA premiums on Executive's behalf would result in a violation of applicable law (including, but not limited to, the 2010 Patient Protection and Affordable Care Act, as amended by the 2010 Health Care and Education Reconciliation Act), then in lieu of paying COBRA premiums pursuant to this Section, the Company shall pay Executive on the last day of each remaining month of the COBRA Payment Period, a fully taxable cash payment equal to the COBRA premium for such month, subject to applicable tax withholding, for the remainder of the COBRA Payment Period. Nothing in this Agreement shall deprive Executive of Executive's rights under COBRA or ERISA for benefits under plans and policies arising under Executive's employment by the Company.

(b) Executive shall not receive the Non-CIC Severance Benefits pursuant to Section 6.2(a) unless Executive executes the Separation Agreement within the consideration period specified therein, which shall in no event be more than forty-five (45) days, and until the Separation Agreement becomes effective and can no longer be revoked by Executive under its terms. Executive's ability to receive benefits pursuant to Section 6.2(a) is further conditioned upon Executive: (i) returning all Company property; (ii) complying with Executive's post-termination obligations under this Agreement and the Confidential Information Agreement; (iii) complying with the Separation Agreement, including without limitation any non-disparagement, non-competition, and confidentiality provisions contained therein; and (iv) resignation from any other positions Executive holds with the Company, effective no later than Executive's date of termination (or such other date as requested by the Board).

(c) The Company will not make any payments to Executive with respect to any of the benefits pursuant to Section 6.2(a) prior to the 60th day following Executive's date of termination. On the first payroll date after the 60th day following Executive's date of termination, and provided that Executive has delivered an effective Separation Agreement, the Company will make the first payment to Executive under Section 6.2(a)(i) and, in a lump sum, an amount equal to the aggregate amount of payments that the Company would have paid Executive through such date had the payments commenced on Executive's date of termination through such 60th day, with the balance of the payments paid thereafter on the schedule described above, subject to any delay in payment required by Section 6.6.

(d) For purposes of this Agreement, "***Accrued Obligations***" are (i) Executive's accrued but unpaid salary through the date of termination and, if required by applicable law and the Company's applicable policy as of the time of termination, any accrued but unused vacation through the date of termination (both of which, for purpose of clarity, shall be paid in cash), (ii) any unreimbursed business expenses incurred by Executive payable in accordance with the Company's standard expense reimbursement policies, and (iii) benefits owed to Executive under any qualified retirement plan or health and welfare benefit plan in which Executive was a participant in accordance with applicable law and the provisions of such plan.

(e) For purposes of this Agreement, "***Good Reason***" means any of the following actions taken by the Company without Executive's express prior written consent: (i) a material reduction by the Company of Executive's Base Salary (other than in a broad based reduction similarly affecting all other members of the Company's executive management); (ii) the relocation of Executive's principal place of employment, without Executive's consent, to a place that increases Executive's one-way commute by more than fifty (50) miles as compared to Executive's then-current principal place of employment immediately prior to such relocation; or (iii) a material reduction in Executive's duties, authority, or responsibilities for the Company relative to Executive's duties, authority, or responsibilities in effect immediately prior to such reduction; provided, however, that, any such termination by Executive shall only be deemed for Good Reason pursuant to this definition if: (1) Executive gives the Company written notice of Executive's intent to terminate for Good Reason within thirty (30) days following Executive's learning of the occurrence of the condition(s) that Executive believes constitute(s) Good Reason, which notice shall describe such condition(s); (2) the Company fails to remedy such condition(s) within thirty (30) days following receipt of the written notice (the "***Cure Period***"); and (3) Executive voluntarily terminates Executive's employment within thirty (30) days following the end of the Cure Period.

(f) For purposes of this Agreement, "***Cause***" means (i) a material breach of any covenant or condition under this Agreement or any other agreement between the parties; (ii) any act constituting dishonesty, fraud, immoral or disreputable conduct which is reasonably likely to cause harm (including reputational harm) to the Company; (iii) any conduct which constitutes a felony under applicable law; (iv) material violation of any Company policy (including but not limited to Company policies preventing harassment), after the expiration of thirty (30) days without cure after written notice of such violation to the extent such violation is curable; (v) refusal to follow or implement a clear, lawful and reasonable directive of Company after the expiration of thirty (30) days without cure after written notice of such failure to the extent such failure is curable; (vi) gross negligence or incompetence in the performance of Executive's duties after the expiration of thirty (30) days without cure after written notice of such failure; or (vii) breach of fiduciary duty.

(g) The benefits provided to Executive pursuant to this Section 6.2 are in lieu of, and not in addition to, any benefits to which Executive may otherwise be entitled under any Company severance plan, policy, or program.

(h) Any damages caused by the termination of Executive's employment without Cause or for Good Reason would be difficult to ascertain; therefore, the Non-CIC Severance Benefits for which Executive is eligible pursuant to Section 6.2(a) above in exchange for the Separation Agreement is agreed to by the parties as liquidated damages, to serve as full compensation, and not a penalty.

(i) If the Company terminates Executive's employment for Cause, or Executive resigns from employment with the Company without Good Reason, regardless of whether or not such termination is in connection with a Change in Control, then Executive shall be entitled to the Accrued Obligations, but Executive will not receive the Non-CIC Severance Benefits, the CIC Severance Benefits, or any other severance compensation or benefit.

6.3 Resignation by Executive for Good Reason or Termination by the Company without Cause (in connection with a Change in Control).

(a) In the event that the Company terminates Executive's employment without Cause or Executive resigns for Good Reason within twelve (12) months following the effective date of a Change in Control ("***Change in Control Termination Date***"), then Executive shall be entitled to the Accrued Obligations and, subject to Executive's compliance with Section 6.2(b) above, Executive shall be eligible to receive the following severance benefits (collectively the "***CIC Severance Benefits***"), subject to the terms and conditions set forth in Section 6.3(b):

(i) An amount equal to twelve (12) months of Executive's then current Base Salary, less standard payroll deductions and withholdings, paid in installments on the Company's regular payroll dates; and

(ii) Provided Executive or Executive's covered dependents, as the case may be, timely elects continued coverage under COBRA under the Company's group health plans following such termination, the portion of the COBRA premiums which is equal to the cost of the coverage that the Company was paying as of the date of termination, to continue Executive's (and Executive's covered dependents, as applicable) health insurance coverage in effect on the termination date until the earliest of: (1) twelve (12) months following the termination date; (2) the date when Executive becomes eligible for substantially equivalent health insurance coverage in connection with new employment or self-employment; or (3) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination (such period from the termination date through the earlier of (1)-(3), (the "***CIC COBRA Payment Period***"). Notwithstanding the foregoing, if at any time the Company determines that its payment of COBRA premiums on Executive's behalf would result in a violation of applicable law (including, but not limited to, the 2010 Patient Protection and Affordable Care Act, as amended by the 2010 Health Care and Education Reconciliation Act), then in lieu of paying COBRA premiums pursuant to this Section, the Company shall pay Executive on the last day of each remaining month of the CIC COBRA Payment Period, a fully taxable cash payment equal to the COBRA premium for such month, subject to applicable tax withholding, for the remainder of the CIC COBRA Payment Period. Nothing in this Agreement shall deprive Executive of Executive's rights under COBRA or ERISA for benefits under plans and policies arising under Executive's employment by the Company;

(iii) A lump sum cash payment in an amount equal to the full Annual Bonus calculated at the Target Percentage for the year in which the termination occurs, subject to standard payroll deductions and withholdings; and

(iv) Effective as of Executive's Change in Control Termination Date (and notwithstanding anything to the contrary in the applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such equity awards), the vesting and exercisability of all outstanding equity awards held by Executive immediately prior to the Change in Control Termination Date shall be accelerated in full, and otherwise shall be administered in accordance with the applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such equity awards.

(b) The Company will not make any payments to Executive with respect to any of the benefits pursuant to Section 6.3(a) prior to the 60th day following Executive's date of termination. On the first payroll date after the 60th day following Executive's date of termination, and provided that Executive has delivered an effective Separation Agreement, the Company will (i) make the first payment to Executive under Section 6.2(a)(i) and, in a lump sum, an amount equal to the aggregate amount of payments that the Company would have paid Executive through such date had the payments commenced on Executive's date of termination through such 60th day, with the balance of the payments paid thereafter on the schedule described above; and (ii) make the lump sum payment specified in Section 6.3(a)(iii) that has not yet been made due to this Section 6.3(b), in the cases of (i) and (ii) subject to any delay in payment required by Section 6.6.

(c) The benefits provided to Executive pursuant to this Section 6.3 are in lieu of, and not in addition to, any benefits to which Executive may otherwise be entitled under any Company severance plan, policy, or program. For avoidance of doubt, Executive shall not be eligible for both CIC Severance and Non-CIC Severance.

(d) Any damages caused by the termination of Executive's employment without Cause or for Good Reason in connection with a Change in Control would be difficult to ascertain; therefore, the CIC Severance Benefits for which Executive is eligible pursuant to Section 6.3(a) above in exchange for the Separation Agreement is agreed to by the parties as liquidated damages, to serve as full compensation, and not a penalty.

6.4 **Cooperation With the Company After Termination of Employment**. Following termination of Executive's employment for any reason, Executive shall reasonably cooperate with the Company in all matters relating to the winding up of Executive's pending work including, but not limited to, any litigation in which the Company is involved, and the orderly transfer of any such pending work to such other executives as may be designated by the Company; provided, that the Company agrees that the Company (a) shall make reasonable efforts to minimize disruption of Executive's other activities, and (b) shall reimburse Executive for all reasonable expenses incurred in connection with such cooperation.

6.5 **Effect of Termination.** Executive agrees that should Executive's employment be terminated for any reason, Executive shall be deemed to have resigned from any and all positions with the Company, including, but not limited to, a position on the Board and all positions with any and all subsidiaries and Affiliates of the Company.

6.6 **Application of Section 409A**.

(a) It is intended that all of the compensation payable under this Agreement, to the greatest extent possible, either complies with the requirements of Section 409A of the Code and the regulations and other guidance thereunder and any state law of similar effect (collectively, "***Section 409A***") or satisfies one or more of the exemptions from the application of Section 409A, and this Agreement will be construed in a manner consistent with such intention, incorporating by reference all required definitions and payment terms.

(b) No severance payments will be made under this Agreement unless Executive's termination of employment constitutes a Separation from Service. For purposes of

Section 409A (including, without limitation, for purposes of Treasury Regulations Section 1.409A-2(b)(2)(iii)), Executive's right to receive any installment payments under this Agreement (whether severance payments or otherwise) shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment hereunder shall at all times be considered a separate and distinct payment.

(c) To the extent that any severance payments are deferred compensation under Section 409A, and are not otherwise exempt from the application of Section 409A, then, to the extent required to comply with Section 409A, if the period during which Executive may consider and sign the Separation Agreement spans two calendar years, the severance payments will not begin until the second calendar year. If the Company determines that the severance benefits provided under this Agreement constitutes "deferred compensation" under Section 409A and if Executive is a "specified employee" of the Company, as such term is defined in Section 409A(a)(2)(B)(i) of the Code at the time of Executive's Separation from Service, then, solely to the extent necessary to avoid the incurrence of the adverse personal tax consequences under Section 409A, the timing of the severance will be delayed as follows: on the earlier to occur of (a) the date that is six months and one day after Executive's Separation from Service, and (b) the date of Executive's death, the Company will: (i) pay to Executive a lump sum amount equal to the sum of the severance benefits that Executive would otherwise have received if the commencement of the payment of the severance benefits had not been delayed pursuant to this Section 6.6(c); and (ii) commence paying the balance of the severance benefits in accordance with the applicable payment schedule set forth in Sections 6.2 and 6.3. No interest shall be due on any amounts deferred pursuant to this Section 6.6(c).

(d) To the extent required to avoid accelerated taxation and/or tax penalties under Section 409A, amounts reimbursable to Executive under this Agreement shall be paid to Executive on or before the last day of the year following the year in which the expense was incurred and the amount of expenses eligible for reimbursement (and in-kind benefits provided to Executive) during any one year may not effect amounts reimbursable or provided in any subsequent year. The Company makes no representation that compensation paid pursuant to the terms of this Agreement will be exempt from or comply with Section 409A and makes no undertaking to preclude Section 409A from applying to any such payment.

6.7 <u>Excise Tax Adjustment</u>.

(a) If any payment or benefit Executive will or may receive from the Company or otherwise (a "***280G Payment***") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this Section, be subject to the excise tax imposed by Section 4999 of the Code (the "***Excise Tax***"), then any such 280G Payment provided pursuant to this Agreement (a "***Payment***") shall be equal to the Reduced Amount. The "***Reduced Amount***" shall be either (x) the largest portion of the Payment that would result in no portion of the Payment (after reduction) being subject to the Excise Tax, or (y) the largest portion, up to and including the total, of the Payment, whichever amount (i.e., the amount determined by clause (x) or by clause (y)), after taking into account all applicable federal, state, and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in Executive's receipt, on an after-tax basis, of the greater economic benefit notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in a Payment is required pursuant to the preceding sentence and the Reduced Amount is determined pursuant to clause (x) of

the preceding sentence, the reduction shall occur in the manner (the "***Reduction Method***") that results in the greatest economic benefit for Executive. If more than one method of reduction will result in the same economic benefit, the items so reduced will be reduced pro rata (the "***Pro Rata Reduction Method***").

(b) Notwithstanding any provision of this Section 6.7 to the contrary, if the Reduction Method or the Pro Rata Reduction Method would result in any portion of the Payment being subject to taxes pursuant to Section 409A that would not otherwise be subject to taxes pursuant to Section 409A, then the Reduction Method and/or the Pro Rata Reduction Method, as the case may be, shall be modified so as to avoid the imposition of taxes pursuant to Section 409A as follows: (A) as a first priority, the modification shall preserve to the greatest extent possible, the greatest economic benefit for Executive as determined on an after-tax basis; (B) as a second priority, Payments that are contingent on future events (*e.g.*, being terminated without Cause), shall be reduced (or eliminated) before Payments that are not contingent on future events; and (C) as a third priority, Payments that are "deferred compensation" within the meaning of Section 409A shall be reduced (or eliminated) before Payments that are not deferred compensation within the meaning of Section 409A.

(c) Unless Executive and the Company agree on an alternative accounting firm or law firm, the accounting firm engaged by the Company for general tax compliance purposes as of the day prior to the effective date of the Change in Control transaction shall perform the foregoing calculations. If the accounting firm so engaged by the Company is serving as accountant or auditor for the individual, entity, or group effecting the Change in Control transaction, the Company shall appoint a nationally recognized accounting or law firm to make the determinations required by this Section 6.7. The Company shall bear all expenses with respect to the determinations by such accounting or law firm required to be made hereunder. The Company shall use commercially reasonable efforts to cause the accounting or law firm engaged to make the determinations hereunder to provide its calculations, together with detailed supporting documentation, to Executive and the Company within fifteen (15) calendar days after the date on which Executive's right to a 280G Payment becomes reasonably likely to occur (if requested at that time by Executive or the Company) or such other time as requested by Executive or the Company.

(d) If Executive receives a Payment for which the Reduced Amount was determined pursuant to clause (x) of Section 6.7(a) and the Internal Revenue Service determines thereafter that some portion of the Payment is subject to the Excise Tax, Executive agrees to promptly return to the Company a sufficient amount of the Payment (after reduction pursuant to clause (x) of Section 6.7(a)) so that no portion of the remaining Payment is subject to the Excise Tax. For the avoidance of doubt, if the Reduced Amount was determined pursuant to clause (y) of Section 6.7(a), Executive shall have no obligation to return any portion of the Payment pursuant to the preceding sentence.

7. GENERAL PROVISIONS.

7.1 **Notices**. Any notices required hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by electronic mail or confirmed facsimile if sent during normal business hours of the recipient, and if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally

recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the Company at its primary office location and to Executive at Executive's address as listed on the Company payroll or (if notice is given prior to Executive's termination of employment) to Executive's Company-issued email address, or at such other address as the Company or Executive may designate by ten (10) days' advance written notice to the other.

7.2 Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal, or unenforceable in any respect under any applicable law or rule in any jurisdiction, such invalidity, illegality, or unenforceability will not affect any other provision or any other jurisdiction, but this Agreement will be reformed, construed, and enforced in such jurisdiction as if such invalid, illegal, or unenforceable provisions had never been contained herein.

7.3 Waiver. If either party should waive any breach of any provisions of this Agreement, Executive or the Company shall not thereby be deemed to have waived any preceding or succeeding breach of the same or any other provision of this Agreement.

7.4 Complete Agreement. This Agreement (including Exhibits A and B), and any other separate agreement relating to equity awards constitute the entire agreement between Executive and the Company with regard to the subject matter hereof and supersede any prior oral discussions or written communications and agreements, including the Prior Agreements. This Agreement is entered into without reliance on any promise or representation other than those expressly contained herein, and it cannot be modified or amended except in writing signed by Executive and an authorized officer of the Company.

7.5 Counterparts. This Agreement may be executed by electronic transmission and in separate counterparts, any one of which need not contain signatures of more than one party, but all of which taken together will constitute one and the same Agreement.

7.6 Headings. The headings of the sections hereof are inserted for convenience only and shall not be deemed to constitute a part hereof nor to affect the meaning thereof.

7.7 Successors and Assigns. The Company shall assign this Agreement and its rights and obligations hereunder in whole, but not in part, to any company or other entity with or into which the Company may hereafter merge or consolidate or to which the Company may transfer all or substantially all of its assets, if in any such case said company or other entity shall by operation of law or expressly in writing assume all obligations of the Company hereunder as fully as if it had been originally made a party hereto, but may not otherwise assign this Agreement or its rights and obligations hereunder. Executive may not assign or transfer this Agreement or any rights or obligations hereunder, other than to Executive's estate upon Executive's death.

7.8 Choice of Law. All questions concerning the construction, validity, and interpretation of this Agreement will be governed by the laws of the Commonwealth of Massachusetts.

7.9 **Resolution of Disputes**. To ensure the timely and economical resolution of disputes that may arise in connection with Executive's employment with the Company, Executive and the Company agree that any and all disputes, claims, or causes of action arising from or relating to the enforcement, breach, performance, negotiation, execution, or interpretation of this Agreement, or Executive's employment, or the termination of Executive's employment, including but not limited to all statutory claims, will be resolved pursuant to the Federal Arbitration Act, 9 U.S.C. §1-16, and to the fullest extent permitted by law, by final, binding and confidential arbitration by a single arbitrator conducted in Boston, Massachusetts by Judicial Arbitration and Mediation Services Inc. ("JAMS") under the then applicable JAMS rules (at the following web address: https://www.jamsadr.com/rules-employment-arbitration/); provided, however, this arbitration provision shall not apply to sexual harassment claims to the extent prohibited by applicable law. A hard copy of the rules will be provided to Executive upon request. **By agreeing to this arbitration procedure, both Executive and the Company waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding.** In addition, all claims, disputes, or causes of action under this provision, whether by Executive or the Company, must be brought in an individual capacity, and shall not be brought as a plaintiff (or claimant) or class member in any purported class or representative proceeding, nor joined or consolidated with the claims of any other person or entity. The arbitrator may not consolidate the claims of more than one person or entity, and may not preside over any form of representative or class proceeding. To the extent that the preceding sentences regarding class claims or proceedings are found to violate applicable law or are otherwise found unenforceable, any claim(s) alleged or brought on behalf of a class shall proceed in a court of law rather than by arbitration. The Company acknowledges that Executive will have the right to be represented by legal counsel at any arbitration proceeding. Questions of whether a claim is subject to arbitration under this Agreement shall be decided by the arbitrator. Likewise, procedural questions which grow out of the dispute and bear on the final disposition are also matters for the arbitrator. The arbitrator shall: (a) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be permitted by law; (b) issue a written arbitration decision, to include the arbitrator's essential findings and conclusions and a statement of the award; (c) be authorized to award any or all remedies that Executive or the Company would be entitled to seek in a court of law; and (d) is authorized to award attorneys' fees to the prevailing party. Subject to the foregoing sentence, the Company shall bear all JAMS' arbitration fees, and each party is responsible for its own attorneys' fees. Nothing in this Agreement is intended to prevent either Executive or the Company from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration. Any awards or orders in such arbitrations may be entered and enforced as judgments in the federal and state courts of any competent jurisdiction. To the extent applicable law prohibits mandatory arbitration of sexual harassment claims, in the event Executive intends to bring multiple claims, including a sexual harassment claim, the sexual harassment claim may be publicly filed with a court, while any other claims will remain subject to mandatory arbitration.

[Remainder of page intentionally left blank.]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Employment Agreement on the day and year first written above.

BICYCLE THERAPEUTICS INC.

By: /s/ Lee Kalowski
Name: Lee Kalowski
Title: President & CFO

EXECUTIVE:

/s/ Nicholas Keen
Nicholas Keen

Exhibit A

CHANGE IN CONTROL

"**Change in Control**" means and includes each of the following:

(a) a Sale; or
(b) a Takeover.

The Compensation Committee of the Board of BTL shall have full and final authority, which shall be exercised in its sole discretion, to determine conclusively whether a Change in Control has occurred pursuant to the above definition, the date of the occurrence of such Change in Control and any incidental matters relating thereto; provided that any such Change in Control also qualifies as a "change in control event" as defined in Section 409A of the United States Internal Revenue Code of 1986, as amended and the regulations and other guidance thereunder and any state law of similar effect, and any exercise of authority in conjunction with a determination of whether a Change in Control is a "change in control event" is consistent with such regulation.

"**Control**" shall have the meaning given to that word by Section 719 of the UK Income Tax (Earnings and Pensions) Act 2003 and "**Controlled**" shall be construed accordingly.

"**Sale**" means the sale of all or substantially all of the assets of BTL.

"**Takeover**" means circumstances in which any person (or a group of persons acting in concert) (the "**Acquiring Person**"):

(a) obtains Control of BTL as the result of making a general offer to:-
  i. acquire all of the issued ordinary share capital of BTL, which is made on a condition that, if it is satisfied, the Acquiring Person will have Control of BTL; or
  ii. acquire all of the shares in BTL; or
(b) obtains Control of BTL as a result of a compromise or arrangement sanctioned by a court under Section 899 of the UK Companies Act 2006, or sanctioned under any other similar law of another jurisdiction; or
(c) becomes bound or entitled under Sections 979 to 985 of the UK Companies Act 2006 (or similar law of another jurisdiction) to acquire shares in BTL or
(d) obtains Control of BTL in any other way, including but not limited to by way of a merger.

Exhibit B

EMPLOYEE CONFIDENTIAL INFORMATION, INVENTIONS, NON-SOLICITATION AND NON-COMPETITION AGREEMENT

DATED 26 September 2019

BicycleTX Ltd

and

Nigel Crockett

SERVICE AGREEMENT

THIS AGREEMENT is made on 26 September 2019

BETWEEN:

(1) **BICYCLETX LIMITED** a company incorporated under the laws of England and Wales (Company Number 11036101) whose registered office is at Building 900 Babraham Research Campus, Babraham, Cambridgeshire, CB22 3AT, United Kingdom (the "**Company**"); and

(2) **NIGEL CROCKETT** of (the "**Employee**").

IT IS AGREED as follows:

1. COMMENCEMENT OF EMPLOYMENT

1.1 This Agreement shall take effect 26th September 2019 (the "**Effective Date**").

1.2 Your employment shall commence on 26th September 2019 and shall continue unless and until either party gives notice to the other in accordance with paragraph 11 below. No employment with a previous employer is deemed to be continuous with your employment with the Company.

1.3 You warrant that by entering into this Agreement or any other arrangements with the Company you will not be in breach of or subject to any express or implied terms of any contract with, or other obligation to, any third party binding on you, including, without limitation, any notice period or the provisions of any restrictive covenants or confidentiality obligations arising out of any employment with any other employer or former employer.

1.4 You warrant that you have the right to work in the United Kingdom and you agree to provide to the Company copies of all relevant documents in this respect at the request of the Company. If at any time during the course of this Agreement you cease to have the right to work in the United Kingdom the Company may immediately terminate your employment without payment of compensation.

2. JOB TITLE

2.1 You shall serve as Chief Business Officer ("**CBO**") reporting to the CEO. The nature of the Company's business may result in changes occurring to the content of your role from time to time. You may also be required to carry out such additional or alternative tasks as may from time to time be reasonably required of you consistent with your executive level and job title, provided that these do not fundamentally change or undermine your position.

2.2 You shall faithfully and diligently perform such duties as you are required to undertake from time to time and exclusively devote the whole of your working time, skills, ability and attention to the business of the Company and use your best endeavours to promote the interests and reputation of the Company and (where applicable) any Group Company.

2.3 The Company may require you to carry out work for, or become a director or officer of, any Group Company at any time.

3. PLACE OF WORK

The Company's offices at Building 900, Babraham Research Campus, Babraham, Cambridge,

UK or such other location as the Company may reasonably determine. The CBO position may require extensive international travel on business.

4. REMUNERATION

4.1 Your salary will be USD370,000 per annum paid monthly in arrears on or about the last working day of each month (less statutory and voluntary deductions) ("**Salary**"). Salary will be converted to GBP and paid in GBP based on the USD/GBP Bank of England daily spot exchange rate applicable on the date of this Agreement, with the exchange rate being revised according to the prevailing Bank of England daily spot exchange rate applicable on 1 January of each year. Your Salary will be reviewed annually in accordance with the Company's practices from time to time (which is expected to be by the end of the first quarter of each year). You will be notified in writing of any changes to your Salary or benefits.

4.2 You agree that the Company may deduct from the Salary or any other sum due to you (including any pay in lieu of notice) any amounts due to the Company including, without limitation, any overpayment of salary, loan or advance.

4.3 For the purposes of this Agreement your earned salary shall mean the proportion of your Salary earned by and due to you in each calendar year of employment with the Company ("**Earned Salary**").

4.4 **Annual Performance Bonuses:**

You will be eligible to participate in the Company's discretionary annual performance related bonus scheme to a maximum value of 35% of your Earned Salary in relation to your performance against agreed annual corporate and personal performance objectives as set out below (the "**Annual Performance Bonus**"). That is, if the compensation committee (the "**Compensation Committee**") of the board of directors (the "**Board**") of the Company's parent company, Bicycle Therapeutics plc ("**BTL**") determines that you have completed all such corporate and personal objectives to its satisfaction in a given year, your bonus would be 35% of your Earned Salary in that year, excluding any other bonuses in this offer. Such bonus may be payable in cash or, in whole or in part, in share options in BTL, as agreed by you and the Compensation Committee following notification by you of your preference at least 90 days prior to the normal payment date (and in the case of share options with the appropriate HMRC valuation process (if required by the Compensation Committee) and Board approval so as to be compliant with BTL's share option plan rules), with due consideration for the operational requirements of the Company at that time in your role as CBO.

Any Annual Performance Bonus paid will not be pensionable and are subject to statutory applicable tax and National Insurance deductions. Performance will be assessed by the Compensation Committee at the end of each calendar year, against annual corporate and personal performance objectives agreed between you and the Board at the start of each calendar year, with any such bonus being payable in the first quarter of the following year. Qualification for your Annual Performance Bonus will require that you are employed by the Company (and have not served notice of termination of your employment to the Company) on 31 December of the year to which your bonus entitlement applies.

4.5 **Equity Incentives**

BTL has established the Bicycle Therapeutics 2019 Share Option Plan (the "**Option Plan**").

On or as soon as practicable following the Effective Date, it is intended that you will be granted an option under the Option Plan to acquire 107,417 ordinary shares in the capital of BTL ("**Shares**") (representing approximately 0.6% of the Company's issued share capital as at the Effective Date).

In addition, and conditional on completion of a transaction on terms set out below, you will be granted a second option under the Option Plan, such option being one of:

(a) an option to acquire 44,757 Shares (representing approximately 0.25% of the Company's issued share capital as at the Effective Date) granted as soon as practicable following the completion of a transaction approved by the Board on terms which include an upfront payment of at least USD30,000,000 and per product downstream milestone payments of at least USD300,000,000; or

(b) an option to acquire 22,378 Shares (representing approximately 0.125% of the Company's issued share capital as at the Effective Date) granted as soon as practicable following the completion of a transaction approved by the Board on terms which include an upfront payment of USD24,000,000 and per product downstream milestone payments of USD240,000,000; or

(c) an option to acquire such number of Shares (falling between 0.125% and 0.25% of the Company's issued share capital as at the Effective Date as the Board shall determine in its absolute discretion) granted as soon as practicable following completion of a transaction approved by the Board on terms which include an upfront payment greater than USD24,000,000 but less than USD 30,000,000, and per product downstream milestone payments greater than USD240,000,000 but less than USD 300,000,000.

Any options granted under this paragraph 4.5 shall be subject to (i) the approval of the Board and/or the Compensation Committee; (ii) the rules of the Option Plan (as amended from time to time); and (iii) the terms of the option grant documentation which will be provided to you following such grant.

5 BENEFITS

5.1 The Company currently operates a personal pension plan provided by Scottish Widows Group. The Company will pay a sum equivalent to 12 % of your basic annual earned salary into a personal pension plan selected by the Company. You may make additional contributions if you wish, but this is not mandatory. In the event that you elect, of your own volition, to opt-out of the Company's pension scheme then the Company will pay you in equal monthly instalments in arrears (less statutory deductions) a sum equivalent to the contribution that it would have made into your pension scheme (the "**Cash Equivalent Payment**") less the Employer's National Insurance Contribution cost incurred by the Company as a result of making the Cash Equivalent Payment.

5.2 The Company currently operates a private healthcare scheme and subject to acceptance by the insurer on reasonable terms, you will be entitled to join.

5.3 The Company operates a death in service scheme which you automatically join upon commencement of employment.

5.4 Further details regarding benefits will be provided upon commencement of your employment. The Company reserves the right to replace or supplement any or all of the scheme(s) referred to in this paragraph 5, or to amend them at any time without compensation, provided that equivalent scheme(s) providing a similar level of benefit are put in place.

6 EXPENSES

The Company shall reimburse all reasonable out of pocket expenses properly incurred by you in the performance of the duties under this Agreement including travelling, subsistence and entertainment expenses provided you follow the Company's guidelines/allowances in force at the relevant time and provided that you shall, where reasonably practicable, provide the Company with vouchers, invoices or such other evidence of such expenses as the Company may reasonably require.

7 HOURS OF WORK

7.1 Your normal working hours are Monday to Friday from 9.00 am to 5.30 pm on each working day with one hour for lunch. You will be required to work such other hours as shall be reasonably necessary for you to perform your duties for which no further remuneration is payable.

7.2 By entering into this Agreement you confirm, that in your capacity as Chief Business Officer you may choose or determine the duration of your working time and the working time limits set out in part II of the Working Time Regulations 1998 do not apply to you.

8 HOLIDAYS

8.1 In addition to the usual public holidays you will be entitled to 25 working days paid holiday in each calendar year. The holiday will accrue on a pro rata basis throughout each calendar year.

8.2 Holidays may only be taken at such time or times as are approved beforehand by the CEO, such approval not to be unreasonably withheld or delayed. You must give reasonable notice of proposed holiday dates by e-mailing the CEO or delegated director in advance, for approval.

8.3 The holiday year runs from January to December. With the agreement of the CEO, you may carry forward up to 5 days of untaken holiday into the next holiday year. Any carried over holiday must be taken by the end of March of the following calendar year or will be forfeited and no payment will be made in respect of any days so forfeited. You will not generally be permitted to take more than 10 days holiday at any one time.

8.4 Upon termination of your employment you will receive pay in lieu of accrued but untaken holiday. The Company may deduct an appropriate sum in respect of days taken in excess of your pro rata entitlement from your final remuneration on the basis that one day's holiday will be calculated as 1/260ths of your basic annual salary.

8.5 In the event that notice of termination of this Agreement is served by either party, the Company may require you to take any outstanding holiday during this notice period.

9 SICKNESS AND OTHER ABSENCE

9.1 If you are unable to attend at work by reason of sickness or injury or any unauthorised reason you must inform the Company as soon as possible on the first day of absence (and in any event not later than 11.00 am on the first day of absence) and, in the case of absence of uncertain duration, you must keep the Company regularly informed of your continued absence and your likely date of return. You are expected to observe this rule very strictly since failure to do so will entitle the Company to stop payment in respect of each day you fail to notify the Company.

9.2 If your absence, due to sickness or injury, is for less than seven (7) days, on your return to work you are required to immediately complete a self-certification form available from the Company. If your absence continues for more than seven (7) consecutive days (whether or not working days) you must provide the Company with a doctor's certificate from the seventh consecutive day of sickness or injury. This doctor's certificate must be provided to the Company promptly following the seventh consecutive day of absence. If illness continues after the expiry of the first certificate, further certificates must be provided promptly to cover the whole period of absence.

9.3 Subject to your compliance with the Company's sickness absence procedures (as amended from time to time), the Company may in its sole and absolute discretion pay full salary and contractual benefits during any period of absence due to sickness or injury for up to an aggregate of 3 months in any fifty-two (52) week period (whether such absence is continuous or intermittent in any calendar year). Such payment shall be inclusive of any statutory sick pay due in accordance with applicable legislation in force at the time of absence. The Company may, in its sole and absolute discretion, extend the period of allowance in an individual case if the circumstances so justify. Thereafter, the Company shall pay statutory sick pay or equivalent benefit to which you may be entitled subject to your compliance with the appropriate rules.

9.4 Whether absent from work or not, you may be, but only on reasonable grounds, required to undergo a medical examination by a Company doctor and your consent will be sought for a report to be sent to the Company.

9.5 The payment of sick pay in accordance with this paragraph 9 is without prejudice to the Company's right to terminate this Agreement prior to the expiry of your right to payments.

9.6 In the event you are incapable of performing your duties by reason of injuries sustained wholly or partly as a result of a third party's actions all payments made to you by the Company as salary or sick pay shall to the extent that compensation is recoverable from that third party constitute loans to you and shall be due and owing when and to the extent that you recover compensation for loss of earnings from the third party.

10 GARDEN LEAVE

10.1 After notice of termination has been given by you or the Company, the Company may at its discretion require you, for all or part of your notice period, to comply with any or all of the following instructions:

(a) not to carry out any further work for the Company or for any Group Company;

(b) to remain away from the Company's business premises and those of any Group

Company (unless given written permission to do otherwise);

(c) not to contact any of the Company's clients, suppliers or employees or those of any Group Company without the Company's prior written permission;

(d) to carry out only part of your duties, or to carry out alternative duties or special projects for the Company within your skill set;

(e) to co-operate in the handover of your duties and responsibilities;

(f) to resign from any offices (including as a director) you hold within the Company or any Group Company or by virtue of your employment with us;

(g) to answer, in an honest and helpful way, such questions as the Company may reasonably ask of you;

(h) to keep the Company informed of your whereabouts and contact details and to remain reasonably contactable and available for work.

10.2 During any such period as described in paragraph 10.1 ("**Garden Leave**") the Company may appoint another person to carry out some or all of your duties. You will continue to owe all other duties and obligations (whether express or implied including fidelity and good faith) during Garden Leave and you shall continue to receive full pay and benefits (except that you will not accrue any further entitlement to any cash or equity incentive awards or bonus payments in respect of the Garden Leave period).

10.3 By placing you on Garden Leave, the Company will not be in breach of this Agreement or any implied duty of any kind whatsoever nor will you have any claim against the Company in respect of any such action.

10.4 During any period of Garden Leave you will remain readily contactable and available for work save when on paid holiday taken in accordance with paragraph 8. In the event that you are not available for work having been requested by the Company to do so, you will, notwithstanding any other provision of this Agreement, forfeit any right to salary and contractual benefits.

10.5 During any period of Garden Leave the Company may require you to deliver up any Confidential Information or property of the Company or any Group Company and upon instruction, delete any emails, spreadsheets or other Confidential Information and you will confirm your compliance with this paragraph 10.5 in writing if requested to do so by the Company.

10.6 During any period of Garden Leave the Company may require you to take any outstanding holiday entitlement.

11 NOTICE

11.1 Without prejudice to the Company's right to summarily terminate your employment in accordance with paragraph 11.3 below and your right to summarily terminate your employment for Good Reason in accordance with paragraph 11.4 below, either you or the Company may terminate your employment by giving to the other not less than six months' notice in writing.

11.2 The Company reserves the right in its sole and absolute discretion to give written notice to

terminate your employment forthwith and to make a payment to you in lieu of salary and the benefits set out in paragraph 5 of this Agreement for all or any unexpired part of the notice period. For the avoidance of doubt, any payment in lieu made pursuant to this paragraph 11.2 will not include any element in relation to any payment in respect of (i) any Annual Performance Bonus or (ii) any holiday entitlement that would have otherwise accrued during the period for which the payment in lieu is made. For the further avoidance of doubt, if the Company elects to make a Payment in Lieu after notice of termination has been given by you, this will not constitute a termination by the Company without Cause for the purposes of paragraphs 11.7 and 11.8 below.

11.3 The Company may summarily terminate your employment hereunder (without notice) for Cause. For purposes of this Agreement, "**Cause**" shall mean where you:

(a) commit gross misconduct which includes, but is not limited to, dishonesty, fraud, theft, being under the influence of alcohol or drugs at work, causing actual or threatening physical harm and causing damage to Company property;

(b) commit a material breach or non-observance of your duties or any of the provisions of this Agreement, or materially fail to observe the lawful directions of the Company, or breach any material Company policy or code of conduct, including but not limited to the Company's policy from time to time on matters relating to harassment;

(c) are convicted of a criminal offence (other than an offence under the road traffic legislation in the United Kingdom or elsewhere for which a non-custodial sentence is imposed);

(d) act in a manner which in the reasonable opinion of the Company, brings the Company into disrepute or otherwise prejudices or is in the reasonable opinion of the Company considered likely to prejudice the reputation of the Company;

(e) in the reasonable opinion of the Company, are guilty of any serious negligence in connection with or affecting the business or affairs of the Company;

(f) are unfit to carry out the duties hereunder because of sickness, injury or otherwise for an aggregate period of 26 weeks in any fifty-two (52) week period even if, as a result of such termination, you would or might forfeit any entitlement to benefit from sick pay under paragraph 9.3 above.

Any delay or forbearance by the Company in exercising any right of termination in accordance with this paragraph 11.3 will not constitute a waiver of such right.

11.4 You may summarily terminate your employment hereunder at any time (without notice) for Good Reason after complying with the Good Reason Process. For purposes of this Agreement, "**Good Reason**" shall mean that you have complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in your responsibilities, authority or duties; (ii) a material diminution in your Salary; (iii) a material change in the geographic location at which you provides services to the Company; or (iv) the material breach of this Agreement by the Company. "**Good Reason Process**" shall mean that (i) you reasonably determine in good faith that a "Good Reason" condition has occurred; (ii) you notify the Company in writing of the first occurrence of the Good

Reason condition within 60 days of the first occurrence of such condition; (iii) you cooperate in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "**Cure Period**"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) you terminate your employment (without notice) within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

11.5 Your employment hereunder shall also terminate immediately upon your death.

11.6 If your employment with the Company is terminated for any reason, the Company shall pay or provide to you (or to your authorised representative or estate) (i) any Salary earned through the Termination Date (as defined below); (ii) unpaid expense reimbursements (subject to, and in accordance with, paragraph 6 of this Agreement); and (iii) any vested benefits you may have under any employee benefit plan of the Company through the Termination Date, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans (collectively, the "**Accrued Benefits**").

Severance Pay and Benefits Upon Termination by the Company without Cause or by the Executive for Good Reason outside the Change in Control Period.

11.7 If your employment is terminated on account of your death or by the Company without Cause (being for any reason not covered by paragraph 11.3), or you terminate your employment for Good Reason (as provided in paragraph 11.4), in either case outside of the Change in Control Period, then the Company shall pay you the Accrued Benefits. In addition, subject to (i) your (or your authorised representative or estate signing, if the termination is due to your death) signing a settlement agreement and a separation agreement and release (together the "**Settlement Agreements**") in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities, a reaffirmation of all of your continuing obligations to the Company, including those set forth in paragraphs 13 – 15, and (in the case of the separation agreement and release) and a seven (7) business day revocation period; and (ii) the separation agreement and release becoming irrevocable, all within 60 days after the Termination Date (or such shorter period as set forth in the Settlement Agreements), the Company shall: (A) pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to nine (9) months of your salary as of the Termination Date (which payment shall not be reduced by either the value of any salary paid to you during your notice period or by any payment in lieu of notice made pursuant to paragraph 11.2); and (B) pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the cost to the Company of providing you with the contractual benefits under paragraph 5 for nine (9) months or, at the Company's option, continue to provide you with such benefits for nine (9) months.

Severance Pay and Benefits Upon Termination by the Company without Cause or by the Executive for Good Reason Within the Change in Control Period

11.8 The provisions of this paragraph 11.8 shall apply in lieu of, and expressly supersede, the provisions of paragraph 11.7 regarding severance pay and benefits upon a termination by the Company without Cause or by you for Good Reason if such termination of employment occurs within 12 months after the occurrence of the first event constituting a Change in Control (such period, the "**Change in Control Period**"). These provisions shall terminate and be of no further

force or effect after the Change in Control Period.

(a) Change in Control Period. If during the Change in Control Period your employment is terminated on account of your death or by the Company without Cause (being for any reason not covered by paragraph 11.3) or you terminate your employment for Good Reason (as provided in paragraph 11.4), then, subject to (i) your signing (or your authorised representative or estate signing, if the termination is due to your death) a settlement agreement and a separation agreement and release (together the Settlement Agreements) in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities, a reaffirmation of all of your continuing obligations to the Company, including those set forth in paragraphs 13 – 15, and (in the case of the separation agreement and release) and a seven (7) business day revocation period; and (ii) the separation agreement and release becoming irrevocable, all within 60 days after the Termination Date (or such shorter period as set forth in the Settlement Agreements):

(i) the Company shall pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the sum of (A) your annual salary as of the Termination Date (or your annual salary in effect immediately prior to the Change in Control, if higher) plus (B) your target annual performance bonus amount under the Annual Bonus Plan for the then-current year (the "**Change in Control Payment**"), which payment shall not be reduced by either the value of any salary paid to you during your notice period or by the value of any payment made to you in lieu of notice pursuant to paragraph 11.2;

(ii) the Company shall: pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the cost to the Company of providing you with the contractual benefits under paragraph 5 for twelve (12) months or, at the Company's option, continue to provide you with such benefits for twelve (12) months; and

(iii) notwithstanding anything to the contrary in any applicable option agreement or other stock-based award agreement, all Time-Based Equity Awards shall immediately accelerate and become fully exercisable (for a period determined in accordance with the rules of the applicable equity plan) or nonforfeitable as of the later of (A) the Termination Date or (B) the Accelerated Vesting Date; *provided* that any termination or forfeiture of the unvested portion of such Time-Based Equity Awards that would otherwise occur on the Termination Date in the absence of this Agreement will be delayed until the Effective Date of the Settlement Agreements and will only occur if the vesting pursuant to this subsection does not occur due to the absence of the Settlement Agreements becoming fully effective within the time period set forth therein. Notwithstanding the foregoing, no additional vesting of the Time-Based Equity Awards shall occur during the period between your Termination Date and the Accelerated Vesting Date.

11.9 Definitions. For purposes of this paragraph 11, the following terms shall have the following meanings:

"**Accelerated Vesting Date**" means the effective date of the Settlement Agreements signed by you (or your authorised representatives or estate if the termination is due to your death).

"**Termination Date**" means the date on which your employment hereunder terminates.

"**Time-Based Equity Awards**" means all time-based stock options and other stock-based awards subject to time based vesting held by you.

"**Change in Control**" has the meaning given to that term in the Schedule to this Agreement.

12 DISCIPLINARY, DISMISSAL AND GRIEVANCE PROCEDURES

12.1 A copy of the Company's disciplinary, dismissal and grievance procedures are set out in its employee handbook (the "**Employee Handbook**").

12.2 Any grievance concerning your employment should be taken up orally in the first instance with the CEO. If the grievance is not resolved to your satisfaction, you should then refer it to the Chairman.

12.3 The Company reserves the right to suspend you on full pay and benefits at any time for a reasonable period to investigate any potential disciplinary matter that it reasonably believes you may be or may have been involved in.

13 OUTSIDE EMPLOYMENT, CONFIDENTIAL INFORMATION, CONFLICTING INTERESTS AND RETURN OF COMPANY PROPERTY

13.1 For the purposes of this paragraph 13, paragraph 10 above and paragraph 14 below the expression "**Confidential Information**" shall include, but not be limited to, any and all knowledge, data or information (whether or not recorded in documentary form or on computer disk or tape), which may be imparted in confidence or which is of a confidential nature or which you may reasonably regard as being confidential or a trade secret by the Company, concerning the business, business performance or prospective business, financial information or arrangements, plans or internal affairs of the Company, any Group Company or any of their respective customers. By way of illustration but not limitation, "**Confidential Information**" includes (a) trade secrets, inventions, mask works, ideas, processes, formulas, software in source or object code, data, records, reports, interpretations, the contents of any databases, programs, other works of authorship, know-how, materials, improvements, discoveries, developments, technical information, designs and techniques and any other proprietary technology and all IPRs (as defined below) therein (collectively, "**Inventions**"); (b) information regarding research, development, new products, planned products, planned surveys, marketing surveys, research reports, market share and pricing statistics, marketing and selling, business plans, financial details, budgets and unpublished financial statements, licenses, prices and costs, fee levels, margins, discounts, credit terms, pricing and billing policies, quoting procedures, commissions, commission charges, other price sensitive information, methods of obtaining business and other business methods, forecasts, future plans and potential strategies, financial projections and business strategies and targets, operational plans, financing and capital-raising plans, activities and agreements, internal services and operational manuals, methods of conducting Company business, corporate and business accounts, suppliers and supplier information, and purchasing; (c) information regarding clients or customers and potential clients or customers of the Company, including customer lists, client

lists, names, addresses (including email), telephone, facsimile or other contact numbers and contact names, representatives, their needs or desires with respect to the types of products or services offered by the Company, proposals, bids, contracts and their contents and parties, the type and quantity of products and services provided or sought to be provided to customers and potential customers of the Company and other non-public information relating to customers and potential customers; (d) information regarding any of the Company's business partners and their services, including names, representatives, proposals, bids, contracts and their contents and parties, the type and quantity of products and services received by the Company, and other non-public information relating to business partners; (e) information regarding personnel, computer passwords, employee lists, compensation and remuneration, and employee skills; and (f) any other non-public information which a competitor of the Company could use to the competitive disadvantage of the Company.

13.2 You shall not, without the prior written consent of the Company, either solely or jointly, directly or indirectly, carry on or be engaged, concerned or interested in any other trade or business, including, but not limited to, carrying on business with the Company's suppliers or dealers, save that nothing in this paragraph 13.2 shall prevent you from holding (with the prior written consent of the Company, which shall not be unreasonably delayed or withheld) up to three percent (3%) of the issued equity share capital of any company where those equity shares are listed on a recognised investment exchange (as defined in section 285 of the Financial Services and Markets Act 2000) or traded on the AIM market operated by the London Stock Exchange. Failure to secure advance permission in accordance with this paragraph 13.2 may result in summary dismissal.

13.3 You will not (except with the prior written consent of the Board) except in the proper course of your duties during the continuance of this Agreement (which for the avoidance of doubt shall include the use of laptops and remote working), or at any time thereafter:

(a) disclose or use for your own or for another's purpose or benefit any Confidential Information which you may learn while in the employment of the Company except as required by a court of law or any regulatory body or that which may be in or become part of the public domain other than through any act or default on your part;

(b) copy or reproduce in any form or by or on any media or device or allow others access to copy or reproduce any documents (including without limitation letters, facsimiles and memoranda), disks, memory devices, notebooks, tapes or other medium whether or not eye-readable and copies thereof on which Confidential Information may from time to time be recorded or referred to ("**Documents**"); or

(c) remove or transmit from the Company or any Group Company's premises any Documents on which Confidential information may from time to time be recorded.

13.4 Upon termination of your employment for any reason by either party, you must immediately return to the Company all Company property including but not limited to documents, papers, records, keys, credit cards, mobile telephones, computer and related equipment, PDA or similar device, security passes, accounts, specifications, drawings, lists, correspondence, catalogues or the like relating to the Company's business which is in your possession or under your control and you must not take copies of the same without the Company's express written authority.

14 RESTRICTIVE COVENANTS

14.1 For the purpose of this paragraph 14 the following expressions shall have the following meanings:

"**Prospective Customer**" shall mean any person, firm, company or other business who was to your knowledge at the Termination Date negotiating with the Company or with any Group Company with a view to dealing with the Company or any Group Company as a customer;

"**Restricted Business**" means any business which (i) carries on research in the field of constrained peptides, including, without limitation, all work in the field of lead constrained peptide identification and optimization and pre-clinical development of constrained peptide therapeutics or (ii) is developing a drug conjugate compound for treating cancer that targets the same target as a drug conjugate compound in development by any Group Company;

"**Restricted Customers**" shall mean any person, firm, company or other business who was to your knowledge at any time in the twelve (12) month period ending with the Termination Date a customer of the Company or any Group Company;

"**Restricted Period**" shall mean the period of twelve (12) months from the Termination Date;

"**Restricted Territory**" means anywhere in the United States or the United Kingdom or in any other country in which the Company or any Group Company conducts business or as of the date of termination of my employment relationship had plans to conduct business; and

"**Termination Date**" shall mean the date on which your employment under this Agreement terminates either due to you or the Company terminating it in accordance with the terms of the Agreement or in breach of the terms of this Agreement.

14.2 During the course of your employment hereunder you are likely to obtain Confidential Information relating to the business of the Company or any Group Company and personal knowledge and influence over clients, customers and employees of the Company or any Group Company. You hereby agree with the Company that to protect the Company's and any and all Group Company's business interests, customer connections and goodwill and the stability of its or their workforce, that you will not during the Restricted Period (and in respect of sub-paragraph 14.2(f) below only, at any time):

(a) in the Restricted Territory, compete with the business of the Company or any Group Company by being directly or indirectly employed or engaged in any capacity by any person, firm or company which engages in or provides Restricted Business or commercial activities competitive with the Restricted Business to Restricted Customers or Prospective Customers;

(b) in the Restricted Territory, compete with the business of the Company or any Group Company either on your own account or for any person, firm or company directly or indirectly by transacting business in competition with the Restricted Business with any Restricted Customer or Prospective Customer of the Company or Group Company and with whom you personally dealt in respect of Restricted Business in the pursuance of the employment hereunder in the twelve (12) months prior to the Termination Date;

(c) in the Restricted Territory, compete with the business of the Company or any Group Company either on your own account or for any person, firm or company directly or indirectly in competition with the Restricted Business by soliciting or endeavouring to solicit or entice the business or custom of any Restricted Customer or Prospective Customer and with whom you personally dealt in respect of Restricted Business in the pursuance of the employment hereunder in the twelve (12) months prior to the Termination Date;

(d) either on your own account or for any person, firm or company directly or indirectly solicit or entice away or endeavour to solicit or entice away any director or senior employee of the Company or any Group Company employed in a managerial, scientific or technical role with whom you have had material personal dealings in the twelve (12) months prior to the Termination Date;

(e) from the Termination Date for the purpose of carrying on any trade, or business represent or allow you to be represented or held out as having any present association with the Company or any Group Company; and

(f) from the Termination Date carry on any trade or business whose name incorporates the word Bicycle or any deviation or extension thereof which is likely or which may be confused with the name of the Company or any Group Company.

14.3 While the restrictions set out in paragraph 14.2 above are considered by the parties to be reasonable in all the circumstances, it is agreed that if any one or more of such restrictions shall either taken by itself or themselves together be adjudged to go beyond what is reasonable in all the circumstances for the protection of the legitimate interests of the Company but would be adjudged reasonable if any particular restriction or restrictions were deleted or if any part or parts of the wording thereof were deleted, restricted or limited in a particular manner, then the restrictions set out in paragraph 14.2 above shall apply with such deletions or restrictions or limitations as the case may be.

14.4 For the avoidance of doubt nothing in this paragraph 14 shall prevent you from having any dealings with any Prospective Customer or Restricted Customer in relation to any business which is not Restricted Businesses and which is not competitive with the Restricted Business, nor from continuing to deal with any Prospective Customer or Restricted Customer where you either have a social or business relationship unconnected to the Company and that relationship does not compete with the Restricted Business.

14.5 The restrictions contained in paragraph 14.2 above are held by the Company for itself and on trust for any other Group Company and shall be enforceable by the Company on their behalf or by any Group Company (at their request). You shall during the employment hereunder enter into direct agreements with any Group Company whereby you will accept restrictions in the same or substantially the same form as those contained in paragraph 14.2 above.

14.6 In the event that the Company exercises its rights and places you on Garden Leave under paragraph 10 above then the Restricted Period shall be reduced by any period/s spent by you on Garden Leave prior to the Termination Date.

14.7 During the Restricted Period you shall provide a copy of the restrictions contained at paragraph 13 above and this paragraph 14 to any employer or prospective employer or any other party

with whom you become or will become engaged or provide service or services to.

15 INTELLECTUAL PROPERTY

15.1 For the purpose of this paragraph 15 "**IPRs**" shall mean all trade secrets, Copyrights, trademarks and trade and business names (including goodwill associated with any trademark or trade or business names and the right to sue for passing off or unfair competition), service marks, mask work rights, patents, petty patents, rights in ideas, concepts, innovations, discoveries, developments and improvements, drug formulations, technology, rights in domain names, rights in inventions, utility models, rights in know-how (including all data, methods, processes, practices and other results of research), unregistered design rights, registered design rights, database rights, semiconductor topography rights and other intellectual property rights recognized by the laws of any jurisdiction or country including all applications and rights to apply for and be granted, renewals or extensions of, and rights to claim priority from, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world; the term "**Copyright**" means the exclusive legal right to reproduce, perform, display, distribute and make derivative works of a work of authorship (as a literary, musical, or artistic work) recognized by the laws of any jurisdiction or country; and the term "**Moral Rights**" means all paternity, integrity, disclosure, withdrawal, special and any other similar rights recognized by the laws of any jurisdiction or country.

15.2 It is contemplated that you may in the course of your employment with the Company create, author or originate (either alone or jointly with others) Inventions (as defined in paragraph 13.1), and/or records, reports, papers, databases, data, information, know how, literature, drawings, graphics, typographical arrangements, designs, works, documents, publications and other materials (in printed, electronic, or any other media or form) (together with Inventions constituting "**Works**").

15.3 You will promptly disclose to the Company full details of any Inventions on their creation and provide further details, explanations and demonstrations as the Company from time to time requests.

15.4 All IPRs subsisting in any Works shall be the exclusive property of the Company.

15.5 To the extent that such IPRs do not vest automatically in the Company by operation of law, you hereby assign and agree to assign to the Company all of your right, title and interest in any existing and future IPRs which may subsist in any Works for their full term of protection (including any extensions, revivals and renewals) together with the right to sue and claim remedies for past infringement and all materials embodying these rights to the fullest extent permitted by law in any and all countries of the world. Insofar as such IPRs do not vest automatically by operation of law or under this Agreement, the Consultant holds legal title in these rights and inventions on trust for the Company.

15.6 To the extent permitted by law you hereby irrevocably and unconditionally waive in favour of the Company, its licensees and successors in title, all existing and future Moral Rights (or similar rights existing in any part of the world) you may have in respect of any Works under Chapter IV of the Copyright Designs and Patents Act 1988 in England or any similar provisions of law in any jurisdiction, including (but without limitation) the right to be identified, the right of integrity and the right against false attribution, and agrees not to institute, support, maintain or

permit any action or claim to the effect that any treatment, exploitation or use of such Works, Inventions or other materials infringes the Consultant's Moral Rights.

15.7 Without prejudice to the generality of paragraph 15.9 below, during your employment with the Company and thereafter, without limit in time, you shall at the request and expense of the Company, promptly assist the Company:

(a) to file, prosecute, obtain and maintain registrations and applications for registration of any IPRs subsisting in, or protecting, any Works; and

(b) to commence and prosecute legal and other proceedings against any third party for infringement of any IPRs subsisting in, or protecting, any Works and to defend any proceedings or claims made by any third party that the use or exploitation of any Works infringes the IPRs or rights of any third party.

15.8 You shall keep details of all Inventions confidential and shall not disclose the subject matter of any Inventions to any person outside the Company without the prior consent of the Company. You acknowledge that any unauthorised disclosure of such subject matter may prevent the Company from obtaining patent or registered intellectual property protection for such Invention.

15.9 Whenever requested to do so by the Company and in any event on the termination or expiry of this Agreement, you shall promptly deliver to the Company all correspondence, documents, papers and records on all media (and all copies or abstracts of them), recording or relating to any part of the Works and the process of their creation which are in your possession, custody or power.

15.10 Subject to paragraph 15.10 below, during your employment with the Company and thereafter without limit in time you shall at the request and expense of the Company promptly execute and do all acts, matters, documents and things necessary or desirable to give the Company the full benefit of the provision of this paragraph 15. You shall not register nor attempt to register any of the IPRs in the Works, nor any of the Inventions, unless requested to do so in writing by the Company.

15.11 Nothing in this paragraph 15 shall be construed, or have the effect of, restricting your rights under sections 39 to 43 (inclusive) of the Patents Act 1977 (as amended from time to time).

16 LITIGATION ASSISTANCE

During the term of your employment and at all times thereafter subject always to your obligations to third parties, you shall furnish such information and proper assistance to the Company or any Group Companies as it or they may reasonably require in connection with the Company's intellectual property (including without limitation applying for, defending, maintaining and protecting such intellectual property) and in connection with litigation in which it is or they are or may become a party. This obligation on you shall include, without limitation, meeting with the Company or any Group Companies' legal advisers, providing witness evidence, both in written and oral form, and providing such other assistance that the Company or any Group Companies' legal advisors in their reasonable opinion determine. The Company shall reimburse you for all reasonable out of pocket expenses incurred by you in furnishing such information and assistance and in the event you are no longer employed by the Company a reasonable daily rate (as agreed between you and the Company for such assistance). Such

assistance shall not require you to provide assistance for more than 5 days in any calendar month. For the avoidance of doubt the obligations under this paragraph 16 shall continue notwithstanding the termination of your employment with the Company.

17 COLLECTIVE AGREEMENTS

There are no collective agreements which directly affect your terms and conditions of employment.

18 DATA PROTECTION

Processing of personal data and our policies

18.1 Information relating to an individual (or from which an individual may be identified) is called "personal data".

18.2 In processing personal data, we are required to comply with the law on data protection. To help us achieve this, we have produced a privacy notice ("**Privacy Notice**"). This may be found in the Employee Handbook. You must read this and comply with it in carrying out your work.

Data protection principles

18.3 In complying with the law on data protection, we are required to comply with what are known as data protection principles. These are summarised in our Privacy Notice. In performing your role and carrying out your responsibilities, you must do your best to ensure that we comply with these principles.

18.4 A key element of the data protection principles is the duty to ensure that data is processed securely and protected against unauthorised or unlawful processing or loss. Key elements include the following:

(a) You must ensure that laptops, memory sticks, phones and other mobile devices are password protected and encrypted. You must not take such devices outside the office without encryption. You must take care of them and keep them secure.

(b) You must use strong passwords, changing them when asked and not sharing them with unauthorised colleagues.

(c) You must not access other individuals' personal data unless in the course of your work.

Data breach – and urgent notification

18.5 If you discover a data breach, you **must** notify the Chairman or CFO immediately – and, if practicable, within one hour. Depending on context, you may then need to provide further information on the circumstances of the breach.

18.6 A data breach occurs where there is destruction, loss, alteration or unauthorised disclosure of or access to personal data which is being held, stored, transmitted or processed in any way. For example, there is a data breach if our servers are hacked or if you lose a laptop or USB stick or send an email to the wrong person by mistake.

18.7 Failure to notify a breach or to provide information as set out above will be treated seriously and disciplinary action may be taken.

Why we process personal data

18.8 For information on the nature of the data we process, why we process it, the legal basis for processing and related matters, please refer to our Privacy Notice. In summary:

(a) We process personal data relating to you for the purposes of our business including management, administrative, employment and legal purposes.

(b) We monitor our premises and the use of our communication facilities, including using CCTV cameras, monitoring compliance with our data and IT policies, and where non-compliance is suspected, looking in a more targeted way.

18.9 The summary above is for information only. We do not, in general, rely on your consent as a legal basis for processing. Agreeing the terms of this Agreement will not constitute your giving consent to our processing of your data.

18.10 We reserve the right to amend the documents referred to above from time to time.

19 THIRD PARTY RIGHTS

Save in respect of any rights conferred by this Agreement on any Group Company (which such Group Company shall be entitled to enforce), a person who is not a party to this Agreement may not under the Contracts (Rights of Third Parties) Act 1999 enforce any of the terms contained within this Agreement.

20 DEFINITIONS

In this Agreement:

"**Group Company**" means a subsidiary or affiliate and any other company which is for the time being a holding company of the Company or another subsidiary or affiliate of any such holding company as defined by the Companies Act 2006 (as amended) and "**Group Companies**" will be interpreted accordingly.

21 ENTIRE AGREEMENT

These terms and conditions constitute the entire agreement between the parties and supersede any other agreement whether written or oral previously entered into.

22 JURISDICTION AND CHOICE OF LAW

This Agreement shall be governed by and interpreted in accordance with the laws of England and Wales and the parties to this Agreement submit to the exclusive jurisdiction of the Courts of England and Wales in relation to any claim, dispute or matter arising out of or relating to this Agreement.

23 NOTICES

Any notices with respect to this Agreement shall be in writing and shall be deemed given if delivered personally (upon receipt), sent by email or sent by first class post addressed, in the case of the Company, to the Company Secretary at its registered office and in your case, addressed to your address last known to the Company.

Schedule

Definitions

Change in Control: means and includes each of the following:

(a) a Sale; or

(b) a Takeover.

The Compensation Committee shall have full and final authority, which shall be exercised in its sole discretion, to determine conclusively whether a Change in Control has occurred pursuant to the above definition, the date of the occurrence of such Change in Control and any incidental matters relating thereto; provided that any such Change in Control also qualifies as a "change in control event" as defined in Section 409A of the United States Internal Revenue Code of 1986, as amended and the regulations and other guidance thereunder and any state law of similar effect, and any exercise of authority in conjunction with a determination of whether a Change in Control is a "change in control event" is consistent with such regulation.

Control: shall have the meaning given to that word by Section 719 of the UK Income Tax (Earnings and Pensions) Act 2003 and "**Controlled**" shall be construed accordingly.

Sale: the sale of all or substantially all of the assets of BTL.

Takeover: circumstances in which any person (or a group of persons acting in concert) (the "**Acquiring Person**"):

(a) obtains Control of BTL as the result of making a general offer to:-

i. acquire all of the issued ordinary share capital of BTL, which is made on a condition that, if it is satisfied, the Acquiring Person will have Control of BTL; or

ii. acquire all of the shares in BTL; or

(b) obtains Control of BTL as a result of a compromise or arrangement sanctioned by a court under Section 899 of the UK Companies Act 2006, or sanctioned under any other similar law of another jurisdiction; or

(c) becomes bound or entitled under Sections 979 to 985 of the UK Companies Act 2006 (or similar law of another jurisdiction) to acquire shares in BTL; or

(d) obtains Control of BTL in any other way, including but not limited to by way of a merger.

THIS AGREEMENT has been executed and delivered as a deed by or on behalf of the parties on the date written at the top of page 1.

Executed as a Deed by **BICYCLETX LIMITED** acting by a director:

/s/ Kevin Lee (Director)

in the presence of:

/s/ Phil Jeffrey

Witness Name: Phil Jeffrey
Witness Address:

Executed as a Deed by **NIGEL CROCKETT:**

/s/ Nigel Crockett (Nigel Crockett)

in the presence of:

/s/ Paula Barnes

Witness Name: Paula Barnes
Witness Address:

BICYCLE THERAPEUTICS PLC
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY
AS AMENDED THROUGH DECEMBER 17, 2019

This Non-Employee Director Compensation Policy (the "Policy") has been established in order to attract and retain non-employee directors who have the knowledge, skills and experience to serve as a member of the Board of Directors (the "Board") of Bicycle Therapeutics plc (the "Company"). Directors who are employees of the Company or any of its subsidiaries will receive no additional compensation for their service as directors.

All equity awards granted in accordance with this Policy shall be granted under the Company's then-current equity incentive plan (or director equity incentive plan, if any).

A. EQUITY AWARDS

At the next scheduled meeting of the Board or the Compensation Committee, as applicable, following a non-employee director's initial election to the Company's Board, the Board or the Compensation Committee of the Board shall grant such non-employee director an option to purchase 32,000 ordinary shares (the "Initial Grant"). Initial Grants will vest in equal tranches of 1/36th at the end of each calendar month following the date of grant, subject to continued service by the director as of such vesting date.

In addition, in January of each year, the Board or the Compensation Committee of the Board will grant to each non-employee director (other than the Chair) who has not announced an intention either to resign from the Board or not to stand for election at the next annual general meeting of shareholders an option to purchase 16,000 ordinary shares, and the Chair will be granted an option to purchase 32,000 ordinary shares (the "Annual Grant"). If a new non-employee director joins the Board following the date of grant of the Annual Grant in any calendar year, such non-employee director will be granted a pro-rata portion of the next Annual Grant, based on the time between his or her appointment and the date of such Annual Grant. Annual Grants shall be vested in full as of the date of grant.

B. CASH FEES

Each non-employee director will receive an annual cash fee for service on the Board and for service on each committee of which the director is a member. The chairs of the Board and of each committee will receive higher fees for such service. The amounts of the fees paid to each non-employee director for service on the Board and for service on each committee of the board of directors on which the director is a member are as follows:

	Member Annual Fee	Chair Annual Fee
Board of Directors	$ 40,000	£ 5,000
Audit Committee	$ 8,500	$ 20,000
Compensation Committee	$ 6,500	$ 14,000
Nominating and Corporate Governance Committee	$ 4,000	$ 8,000
Strategic Committee	$ 30,000	N/A

These fees are payable in arrears in twelve equal monthly installments, subject to deduction of applicable income tax or national insurance which the Company is required by law to deduct and any other statutory deductions, provided that (i) the amount of such payment shall be prorated for any portion of such month during which the director was not serving and (ii) no fee shall be payable in respect of any period prior to the date of the Company's initial public offering.

C. EXPENSES

The reasonable expenses incurred by non-employee directors in connection with attendance at Board or committee meetings or other Company-related activities will be reimbursed upon submission of appropriate documentation.

D. ADMINISTRATION

This Program shall be administered by the Compensation Committee, which shall have the power to interpret these provisions and approve changes from time to time as it deems appropriate.

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

Exhibit 10.18

DISCOVERY COLLABORATION AND LICENSE

AGREEMENT

between

BICYCLETX LIMITED

and

GENENTECH, INC.

Dated as of February 21, 2020

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DISCOVERY COLLABORATION AND LICENSE AGREEMENT

This Discovery Collaboration and License Agreement (the "**Agreement**") is made and entered into effective as of February 21, 2020 (the "**Effective Date**") by and between BicycleTx Limited, a company incorporated in England and Wales ("**BicycleTx**"), and Genentech, Inc., a Delaware corporation ("**Genentech**"). BicycleTx and Genentech are referred to herein individually as a "**Party**" and collectively as the "**Parties**".

RECITALS

WHEREAS, BicycleTx owns or controls certain intellectual property rights with respect to a proprietary phage display discovery platform and related technology for the identification and optimization of Bicycles (as defined herein) suitable for development and commercialization as therapeutic products;

WHEREAS, the Parties desire to collaborate to conduct certain Discovery Research Activities (as defined herein) to generate Bicycles directed to targets selected by Genentech, and to advance the resulting constructs into further pre-clinical development and potential clinical development and commercialization as product candidates; and

WHEREAS, BicycleTx wishes to grant to Genentech, and Genentech wishes to receive, a license under such intellectual property rights to develop and commercialize products incorporating such Bicycles and resulting constructs in the Territory (as defined herein), in each case in accordance with the terms and conditions set forth below.

NOW, THEREFORE, in consideration of the premises and the mutual promises and conditions hereinafter set forth, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, do hereby agree as follows:

ARTICLE 1
DEFINITIONS

Unless otherwise specifically provided herein, the following terms shall have the following meanings:

1.1 "**Accounting Standards**" means, with respect to a Party and its Affiliates, either (a) International Financial Reporting Standards ("**IFRS**") or (b) United States generally accepted accounting principles ("**GAAP**"), in either case ((a) or (b)) that are used at the applicable time, and as consistently applied, by such Party or any of its Affiliates.

1.2 "**Acquisition**" means, with respect to a Party, a merger, acquisition (whether of all of the stock or all or substantially all of the assets of a Person or any operating or business division of a Person) or similar transaction by or with the Party, other than a Change of Control of the Party.

1.3 "**Additional Discovery Activities**" has the meaning set forth in Section 5.2.

1.4 "**Adverse Ruling**" has the meaning set forth in Section 14.3.2.

1.5 "**Affiliate**" means, with respect to a Party, any Person that, directly or indirectly, through one (1) or more intermediaries, controls, is controlled by or is under common control with such Party. For purposes of this definition, "control" and, with correlative meanings, the terms "controlled by" and "under common control with" means (a) the possession, directly or indirectly, of the power to direct the

management or policies of a Person, whether through the ownership of voting securities, by contract relating to voting rights or corporate governance, or otherwise; or (b) the ownership, directly or indirectly, of more than fifty percent (50%) of the voting securities or other ownership interest of a Person (or, with respect to a limited partnership or other similar entity, its general partner or controlling entity). Anything to the contrary in this paragraph notwithstanding, [***] shall not be deemed an Affiliate of Genentech unless Genentech provides written notice to BicycleTx of its desire to include [***] as Affiliate(s) of Genentech.

1.6 "**Agreement**" has the meaning set forth in the preamble hereto.

1.7 "**Alliance Manager**" has the meaning set forth in Section 4.5.

1.8 "**Antigen Target**" means a Target expressed by cells or tissues of interest and (a) may comprise (but is not limited to) proteins expressed within the tumor microenvironment, by tumor cells, or by immune cells and (b) is intended to provide a localization address rather than a functional and/or immunomodulatory response.

1.9 "**Applicable Law**" means federal, state, local, national and supra-national laws, statutes, rules, and regulations, including any rules, regulations, guidelines, or other requirements enacted by a government authority, including Regulatory Authorities, major national securities exchanges or major securities listing organizations, that may be in effect from time to time during the Term and applicable to the performance by a Party of its obligations, or exercise of its rights, under this Agreement.

1.10 "**Audit Expert**" has the meaning set forth in Section 8.15.

1.11 "**Bankruptcy Code**" has the meaning set forth in Section 14.5.1.

1.12 "**Bicycle**" means a monomeric peptide or peptide derivative crosslinked via a central scaffold to form a conformationally constrained structure with more than one cyclic component.

1.13 "**Bicycle Construct**" means a molecule that contains (a) a Bicycle that is specifically directed to or capable of binding a Modulator Target, with or without (b) a Targeting Arm.

1.14 "**BicycleTx**" has the meaning set forth in the preamble hereto.

1.15 "**BicycleTx Background Know-How**" means all Know-How that (a) is Controlled by BicycleTx or any of its Affiliates on the Effective Date or during the Term as a result of performing activities outside the scope of this Agreement and (b) is [***] for (i) the discovery, validation, characterization, and testing of Bicycle Constructs or (ii) Exploiting any Compound or Licensed Product.

1.16 "**BicycleTx Background Patents**" means all Patents that (a) are Controlled by BicycleTx or any of its Affiliates on the Effective Date or during the Term and (b) solely Cover BicycleTx Background Know-How.

1.17 "**BicycleTx Collaboration Invention**" has the meaning set forth in Section 1.45.

1.18 "**BicycleTx Collaboration Know-How**" means all Collaboration Know-How that is generated by or on behalf of BicycleTx or its Affiliates solely or jointly with a Third Party, including all Know-How in BicycleTx Collaboration Inventions.

1.19 "**BicycleTx Collaboration Patents**" means all Patents that Cover BicycleTx Collaboration Inventions.

1.20 "**BicycleTx Future Independent Targeting Arm**" means any Targeting Arm Controlled by BicycleTx during the Term and developed or acquired by BicycleTx independently of activities under this Agreement.

1.21 "**BicycleTx Future In-License Agreement**" means any agreement entered into during the Term by and between BicycleTx and a Third Party with respect to [***] that are [***] in connection with the Discovery Research Activities, under which Third Party agreement BicycleTx or its Affiliates are required to make payments to such Third Party as a result of practicing such [***], as such agreements may be amended from time-to-time. Notwithstanding the foregoing, [***].

1.22 "**BicycleTx Indemnitees**" has the meaning set forth in Section 13.1.

1.23 "**BicycleTx IP**" has the meaning set forth in Section 7.1.1.

1.24 "**BicycleTx Know-How**" means all BicycleTx Background Know-How, BicycleTx Platform Know-How, BicycleTx Product Know-How, and BicycleTx Collaboration Know-How.

1.25 "**BicycleTx Option**" has the meaning set forth in Section 14.6.1(c).

1.26 "**BicycleTx Other Constructs**" has the meaning set forth in Section 9.4.1(b).

1.27 "**BicycleTx Patents**" means all BicycleTx Background Patents, BicycleTx Platform Patents, BicycleTx Product Patents, and BicycleTx Collaboration Patents.

1.28 "**BicycleTx Platform**" means Know-How, Patents and other intellectual property rights that are Controlled by BicycleTx or any of its Affiliates on the Effective Date or during the Term that claim or Cover (a) [***] Bicycles [***], (b) Bicycles, or any component thereof ([***]) and (c) [***] Bicycles, or components thereof.

1.29 "**BicycleTx Platform Know-How**" means all Know-How that (a) is (i) Controlled by BicycleTx or any of its Affiliates on the Effective Date, or (ii) Controlled by BicycleTx or its Affiliates, or generated in the performance of activities under this Agreement by or on behalf of either Party during the Term, and (b) relates to the BicycleTx Platform or any component of the BicycleTx Platform, but [***] Compound or Licensed Product.

1.30 "**BicycleTx Platform Patents**" means all Patents that (a) are Controlled by BicycleTx or any of its Affiliates on the Effective Date or during the Term and (b) Cover (i) BicycleTx Platform Know-How or (ii) a Platform Invention. For clarity, "BicycleTx Platform Patents" excludes any and all Product Patents.

1.31 "**BicycleTx Product Know-How**" means all Product Know-How that is generated by or on behalf of BicycleTx or its Affiliates, solely or jointly with a Third Party, including all Know-How in Product Inventions solely invented by or on behalf of BicycleTx or its Affiliates.

1.32 "**BicycleTx Product Patents**" means all Patents that Cover Product Invention solely invented by or on behalf of BicycleTx or its Affiliates.

1.33 "**Breach Cure Period**" has the meaning set forth in Section 14.3.1.

1.34 "**Breach Notice**" has the meaning set forth in Section 14.3.1.

1.35 "**Breaching Party**" has the meaning set forth in Section 14.3.1.

1.36 "**Business Day**" means a day other than a Saturday or Sunday on which banking institutions in San Francisco, California and London, England are open for business.

1.37 "**Calendar Quarter**" means each successive period of three (3) calendar months commencing on January 1, April 1, July 1 and October 1, except that the first Calendar Quarter of the Term shall commence on the Effective Date and end on the day immediately prior to the first to occur of January 1, April 1, July 1 or October 1 after the Effective Date, and the last Calendar Quarter shall end on the last day of the Term.

1.38 "**Calendar Year**" means each successive period of twelve (12) calendar months commencing on January 1 and ending on December 31, except that the first Calendar Year of the Term shall commence on the Effective Date and end on December 31 of the year in which the Effective Date occurs and the last Calendar Year of the Term shall commence on January 1 of the year in which the Term ends and end on the last day of the Term.

1.39 "**Change of Control**" means, with respect to a Party: (a) that any Third Party acting alone or as part of a group acquires directly or indirectly the beneficial ownership of any voting securities of such Party, or if the percentage ownership of such Party in the voting securities of such Party is increased through stock redemption, cancellation or other recapitalization, and immediately after such acquisition or increase such Third Party is, directly or indirectly, the beneficial owner of outstanding voting securities representing more than fifty percent (50%) of the total voting power of all of the then outstanding voting securities of such Party; (b) a merger (whether by contract, by statute or by operation of law), consolidation, recapitalization or reorganization of such Party is consummated, other than any such transaction in which stockholders or equity holders of such Party immediately prior to such transaction beneficially own, directly or indirectly, at least fifty percent (50%) of the voting securities of the surviving entity (or its parent entity) immediately following such transaction; (c) that the stockholders or equity holders of such Party approve a plan of complete liquidation of such Party; or (d) the sale or disposition to a Third Party of all or substantially all of such Party's assets taken as a whole. For purposes of this definition, "beneficial ownership" shall have the meaning accorded in the U.S. Securities Exchange Act of 1934 and the rules of the U.S. SEC under this Agreement in effect as of the Execution Date. Notwithstanding the foregoing, (i) a transaction solely to change the domicile of a Party; (ii) the consummation of an initial public offering;

or (iii) any merger or consolidation between a Party and one or more Affiliates shall not constitute a Change of Control.

1.40 "**Change of Control Group**" means, with respect to a Party, the Person or entity, or group of Persons or entities, that is the acquirer of, or successor to, a Party in connection with a Change of Control, together with all of the affiliates of such Persons or entities in each case that are not Affiliates of such Party immediately prior to the closing of such Change of Control of such Party.

1.41 "[***] **Targeting Arm**" means the Genentech Targeting Arm directed to the [***] Antigen Target.

1.42 "**Clinical Data**" means all information with respect to any Discovery Construct or Licensed Product, in each case that is made, collected, or otherwise generated under or in connection with Clinical Studies, including any data (including raw data), reports, and results with respect thereto.

1.43 "**Clinical Trial**" means a human clinical study (a) in which Licensed Product is administered to human subjects and (b) that is designed to (i) establish that a pharmaceutical product is reasonably safe for continued testing; (ii) investigate the safety and efficacy of the pharmaceutical product for its intended use, and to define warnings, precautions and adverse reactions that may be associated with the pharmaceutical product in the dosage range to be prescribed; (iii) support Regulatory Approval of such pharmaceutical product or label expansion of such pharmaceutical product; or (iv) obtain or maintain marketing approval and for a purpose other than to obtain, support or maintain Regulatory Approval, including any and all post-marketing commitments.

1.44 "**CMC Activities**" means, with respect to activities directed to the generation of chemistry, manufacturing and controls information and data for a Licensed Product, Lead Discovery Construct or Development Candidate, as applicable, required by Applicable Law to be included or referenced in, or that otherwise supports, an IND or Drug Approval Application for such Licensed Product.

1.45 "**Collaboration Invention**" means an Invention, other than a Platform Invention, that is first discovered, made, conceived, or reduced to practice under this Agreement. A Collaboration Invention may be discovered, made, conceived or reduced to practice solely by or on behalf of BicycleTx ("**BicycleTx Collaboration Invention**"), solely by or on behalf of Genentech ("**Genentech Collaboration Invention**"), or jointly by or on behalf of BicycleTx and Genentech (whether by such Party's employees or by Third Parties performing services for either Party) ("**Joint Collaboration Invention**").

1.46 "**Collaboration Know-How**" means all Know-How other than BicycleTx Platform Know-How that is generated in the performance of activities under this Agreement, including all Know-How in Collaboration Inventions.

1.47 "**Collaboration Patent**" means a Patent that Covers one or more Collaboration Inventions. For clarity, a Patent that Covers a Collaboration Invention that also incorporates, as applicable BicycleTx Background Know-How or Genentech Background Know-How, will be deemed a Collaboration Patent.

1.48 "**Collaboration Program**" has the meaning set forth in Section 2.1.

1.49 "**Collaboration Target**" means (a) the Initial Collaboration Targets, (b) each Modulator Target for which Genentech exercises its Expansion Option pursuant to Section 3.1.1(b), in each case of (a)

and (b) as may be substituted pursuant to Section 3.2, and (c) each Antigen Target to which a Targeting Arm incorporated within a Discovery Construct pursuant to Section 2.3.2 is directed.

1.50 "**Combination Product**" means (a) a single pharmaceutical formulation containing as its active ingredients both (i) a Compound and (ii) one or more other therapeutically or prophylactically active ingredients that are not Compounds (each such other therapeutically or prophylactically active ingredient, a "**Non-Compound Active Agent**") or (b) a combination therapy comprised of (i) a Compound and (ii) one or more other therapeutically or prophylactically active products containing at least one Non-Compound Active Agent, whether priced and sold together in a single package containing such multiple products or packaged separately but sold together for a single price, in each case (a) and (b), including all dosage forms, formulations, presentations, line extensions, and package configurations.

1.51 "**Commercialization**" means any and all activities directed to the preparation for sale of, offering for sale of, or sale of a Compound or Licensed Product, including activities related to marketing, promoting, selling, distributing, importing and exporting such Compound or Licensed Product, and interacting with Regulatory Authorities regarding any of the foregoing. When used as a verb, "**to Commercialize**" and "**Commercializing**" means to engage in Commercialization, and "**Commercialized**" has a corresponding meaning.

1.52 "**Commercially Reasonable Efforts**" means, with respect to the performance of Development, Commercialization, or Manufacturing activities with respect to a Compound or a Licensed Product, the carrying out of such activities using efforts and resources [***], taking into account [***] would take into account, including [***], the nature and extent of [***] required. For clarity, [***].

1.53 "**Compound**" means any Development Candidate or other Discovery Construct that has met the Discovery Construct Threshold. The term Compound also includes any and all Modified Compounds.

1.54 "**Confidential Information**" means any information provided orally, visually, in writing or other form by or on behalf of one (1) Party (or an Affiliate or representative of such Party) to the other Party (or to an Affiliate or representative of such other Party) in connection with this Agreement, whether prior to, on, or after the Effective Date, including information relating to the terms of this Agreement, the identities of a Collaboration Target (including Genentech Reserved Targets), the Discovery Construct or any Licensed Product (including the Regulatory Documentation and regulatory data), any Exploitation of

any Discovery Construct or any Licensed Product, any Know-How with respect thereto developed by or on behalf of the disclosing Party or its Affiliates, or the scientific, regulatory or business affairs or other activities of either Party. Notwithstanding the foregoing, (a) Joint Collaboration Know-How shall be deemed to be the Confidential Information of both Parties, and both Parties shall be deemed to be the receiving Party and the disclosing Party with respect thereto, and (b) all Regulatory Documentation owned by Genentech pursuant to Section 5.6.1 shall be deemed to be the Confidential Information of Genentech, and Genentech shall be deemed to be the disclosing Party and BicycleTx shall be deemed to be the receiving Party with respect thereto. In addition, all information disclosed by BicycleTx to Genentech under the Non-Disclosure Agreement between the Parties, dated [***], (the "**Prior NDA**") shall be deemed to be BicycleTx's Confidential Information disclosed hereunder, and all information disclosed by Genentech to BicycleTx under the Prior NDA shall be deemed to be Genentech's Confidential Information disclosed hereunder.

1.55 "**Control**" means, with respect to any Know-How, Regulatory Documentation, material, Patent or other property right, the possession of the right, whether directly or indirectly, and whether by ownership, license, covenant not to sue or otherwise (other than by operation of the license and other grants in Sections 7.1 or 7.2), to grant a license, sublicense or other right to or under such Know-How, Regulatory Documentation, material, Patent or other property right, as provided for herein without violating the terms of any agreement or other arrangement with any Third Party.

1.56 "**Cover**" means (as an adjective or as a verb including conjugations and variations such as "**Covered**", "**Coverage**" or "**Covering**"), with respect to a particular subject matter at issue and a relevant Patent, that, in the absence of a license under or ownership of such Patent, the developing, making, using, offering for sale, promoting, selling, exporting or importing of such subject matter would infringe one or more Valid Claims of such Patent or, as to a pending claim included in such Patent, the developing, making, using, offering for sale, promoting, selling, exporting or importing of such subject matter would infringe such Patent if such pending claim were to issue in an issued Patent. The determination of whether any given subject matter is Covered by a particular Valid Claim shall be made on a country-by-country basis.

1.57 "**Development**" means all activities related to research, pre-clinical and other non-clinical testing, test method development and stability testing, toxicology, formulation, process development, manufacturing scale-up, qualification and validation, quality assurance/quality control, Clinical Trials, including Manufacturing in support thereof, statistical analysis and report writing, the preparation and submission of Drug Approval Applications, regulatory affairs with respect to the foregoing and all other activities necessary or reasonably useful or otherwise requested or required by a Regulatory Authority as a condition or in support of obtaining or maintaining a Regulatory Approval. When used as a verb, "**Develop**" means to engage in Development. For purposes of clarity, Development shall include any submissions and activities required in support thereof, required by Applicable Laws or a Regulatory Authority as a condition or in support of obtaining a pricing or reimbursement approval for an approved Licensed Product.

1.58 "**Development Candidate**" has the meaning set forth in Section 2.3.1(d).

1.59 "**Dev Go**" means [***] approval of a Compound (or a program directed to such Compound following the completion of the Lead Validation Phase for commencement of IND-enabling studies [***].

1.60 "**Dev Go Criteria**" means, on a Collaboration Program-by-Collaboration Program basis, the criteria [***] to be achieved by a Discovery Construct in such Collaboration Program at the time of delivery of the Dev Go Data Package. The Dev Go Criteria for the Initial Collaboration Targets as of the Effective Date are set forth on Schedule 1.60.

1.61 "**Dev Go Data Package**" has the meaning set forth in Section 2.5.2(a).

1.62 "**Dev Go Data Package Acceptance Date**" has the meaning set forth in Section 2.5.2(d).

1.63 "**Dev Go Notice**" has the meaning set forth in Section 2.5.2(d)

1.64 "**Dev Go Review Period**" has the meaning set forth in Section 2.5.2(d).

1.65 "**Discovery Construct**" has the meaning set forth in Section 2.3.1(b).

1.66 "**Discovery Construct Threshold**" means, with regard to each Modulator Target, the threshold criteria that Discovery Constructs must meet in order to be included in a LSR Go Data Package and be eligible for further research and development in the subsequent phases of the collaboration, as set forth on Schedule 1.66.

1.67 "**Discovery Phase**" has the meaning set forth in Section 2.3.1.

1.68 "**Discovery Research Activities**" means the research and Development activities set forth in a Discovery Research Plan to be performed by BicycleTx.

1.69 "**Discovery Research Plan**" means the research plan setting forth (a) the activities (and estimated timelines) for (i) for the identification, evaluation and validation of Bicycle Constructs directed to a Collaboration Target suitable for progression as Discovery Constructs, (ii) evaluation, validation and optimization of Targeting Arms directed to Antigen Targets, if requested by Genentech, and (iii) characterization, prioritization and optimization of such Discovery Constructs, [***], to identify and validate one or more lead Discovery Constructs suitable to progress into further pre-clinical and clinical Development, and (b) the data, results and information required to be included in (i) the LSR Go Data Package and (ii) the Dev Go Data Package, in each case ((a) and (b)) including the applicable LSR Go Criteria or Dev Go Criteria and as the same may be amended from time to time in accordance with the terms hereof.

1.70 "**Dispute**" has the meaning set forth in Section 15.7.

1.71 "**Distributor**" has the meaning set forth in Section 7.5.

1.72 "**Dollars**" or "**$**" means United States Dollars.

1.73 "**Drug Approval Application**" means an NDA, or any corresponding foreign application in the Territory, including, with respect to the European Union, a Marketing Authorization Application (a "**MAA**") filed with the EMA or with the applicable Regulatory Authority of a country in Europe with respect to the mutual recognition or any other national approval procedure.

1.74 "**Effective Date**" means the effective date as set forth in the preamble hereto.

1.75 "**EMA**" means the European Medicines Agency and any successor agency(ies) or authority having substantially the same function.

1.76 "**European Major Market**" means [***].

1.77 "**Evaluation Completion Notice**" has the meaning set forth in Section 2.3.1(a).

1.78 "**Evaluation Phase**" has the meaning set forth in Section 2.3.1(a).

1.79 "**Exclusivity Obligations**" has the meaning set forth in Section 7.8.1.

1.80 "**Existing Patents**" has the meaning set forth in Section 12.2.1.

1.81 "**Existing Targeting Arms**" means the Targeting Arms Controlled by BicycleTx as of the Effective Date that are directed to the Antigen Targets set forth on Schedule 1.81.

1.82 "**Expansion Option**" has the meaning set forth in Section 3.1.1(b).

1.83 "**Expansion Option Period**" means the period [***].

1.84 "**Expert**" means a person with no less than [***] experience and expertise having occupied at least one [***], but excluding any and all current or former employees and consultants of either Party. Such person shall be fluent in the English language.

1.85 "**Expert Committee**" has the meaning set forth in Section 1.166.

1.86 "**Exploit**" or "**Exploitation**" means to make, have made, import, export, use, have used, sell, have sold, or offer for sale, including to Develop, Commercialize, register, Manufacture, have Manufactured, hold, or keep (whether for disposal or otherwise), or otherwise dispose of.

1.87 "**FDA**" means the United States Food and Drug Administration and any successor agency(ies) or authority having substantially the same function.

1.88 "**FFDCA**" means the United States Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., as amended from time to time, together with any rules, regulations and requirements promulgated thereunder (including all additions, supplements, extensions, and modifications thereto).

1.89 "**Field**" means all uses.

1.90 "**First Commercial Sale**" means, with respect to a Licensed Product and a country, the first sale for monetary value for use or consumption by the end user of such Licensed Product in such country after Regulatory Approval for such Licensed Product has been obtained in such country. Sales prior to receipt of Regulatory Approval for such Licensed Product, such as so-called "treatment IND sales", "named patient sales", and "compassionate use sales" shall not be construed as a First Commercial Sale.

1.91 "**First-in-Human Clinical Trial**" means the first-ever human Clinical Trial in any country conducted in accordance with good clinical practices (as defined under Applicable Law) that is intended to initially evaluate a Licensed Product with respect to safety, tolerability, pharmacological effects and determination of maximum tolerated dose or recommended dose of such Licensed Product for subsequent human clinical trials as the primary endpoint, or that would otherwise satisfy requirements of 21 CFR 312.21(a), or its foreign equivalent.

1.92 "**FPFD**" means, with respect to a Licensed Product and a Clinical Trial, the first dosing of the first patient with such Licensed Product in such Clinical Trial.

1.93 "**FTE**" means a full-time equivalent person-year, based upon a total of no less than [***] working hours per year, pro-rated as necessary, undertaken in connection with the conduct of research in a Discovery Research Plan. In no circumstance can the work of any given person exceed one (1) FTE.

1.94 "**Future Rights**" has the meaning set forth in Section 9.8.

1.95 "**Gatekeeper**" has the meaning set forth in Section 3.1.5.

1.96 "**Genentech**" has the meaning set forth in the preamble hereto.

1.97 "**Genentech Antigen Target**" has the meaning set forth in Section 2.3.2(d).

1.98 "**Genentech Background Know-How**" means all Know-How that (a) is Controlled by Genentech or any of its Affiliates on the Effective Date or during the Term as a result of performing activities outside the scope of this Agreement and (b) is [***] for Exploiting any Compound or Licensed Product.

1.99 "**Genentech Background Patents**" means all Patents that are (a) Controlled by Genentech or any of its Affiliates on the Effective Date or during the Term and (b) solely Cover Genentech Background Know-How.

1.100 "**Genentech CMC Know-How**" means Genentech Background Know-How and Genentech Collaboration Know-How that is related to CMC Activities.

1.101 "**Genentech Collaboration Invention**" has the meaning set forth in Section 1.45.

1.102 "**Genentech Collaboration Know-How**" means all Collaboration Know-How that is generated by or on behalf of Genentech or its Affiliates solely or jointly with a Third Party, including all Know-How in Genentech Collaboration Inventions.

1.103 "**Genentech Collaboration Patents**" means all Patents that Cover Genentech Collaboration Inventions.

1.104 "**Genentech ESPC**" has the meaning set forth in Section 2.5.2(b).

1.105 "**Genentech Indemnitees**" has the meaning set forth in Section 13.2.

1.106 "**Genentech In-License Agreement**" means any agreement entered into during the Term between Genentech and a Third Party with respect to such [***] for the Exploitation of any Compound (within the limits of the license granted pursuant to Section 7.1) or Licensed Product (excluding any Third Party Patents solely relating to any Non-Compound Active Agent in a Combination Product), and under which Third Party agreement Genentech or its Affiliates are required to make payments to such Third Party as a result of practicing [***] in connection with the Exploitation of a Compound or Licensed Product, including any agreement entered into pursuant to Section 9.8, as such agreements may be amended from time-to-time.

1.107 "**Genentech Know-How**" means all Genentech Background Know-How, Genentech Product Know-How, and Genentech Collaboration Know-How.

1.108 "**Genentech Patents**" means all Genentech Background Patents, Genentech Product Patents, and Genentech Collaboration Patents.

1.109 "**Genentech Product Know-How**" means all Product Know-How that is generated by or on behalf of Genentech or its Affiliates solely or jointly with a Third Party, including all Know-How in Product Inventions solely invented by or on behalf of Genentech or its Affiliates.

1.110 "**Genentech Product Patents**" means Patents that Cover Product Inventions solely invented by or on behalf of Genentech or its Affiliates.

1.111 "**Genentech Reserved Targets**" means the Targets set forth on Schedule 1.111.

1.112 "**Genentech RRC**" has the meaning set forth in Section 2.5.1(b).

1.113 "**Genentech Specified Countries**" has the meaning set forth in Schedule 1.113 and as may be updated by Genentech from time to time through written notification to BicycleTx.

1.114 "**Genentech Targeting Arm of Interest**" has the meaning set forth in Section 2.3.2(c).

1.115 "**Genentech Targeting Arms**" has the meaning set forth in Section 2.3.2(d).

1.116 "**Genentech Withholding Tax Action**" has the meaning set forth in Section 8.11.2.

1.117 "**Generic Entry**" has the meaning set forth in Section 8.7.3(a).

1.118 "**Generic Product**" means, with respect to a particular Licensed Product that has received Regulatory Approval in a regulatory jurisdiction in the Territory and is being marketed and sold by Genentech or any of its Affiliates or Sublicensees in such jurisdiction, a pharmaceutical product that (a) is sold in such jurisdiction by a Third Party that is not an Affiliate, licensee or Sublicensee of Genentech, and did not purchase or acquire such product in a chain of distribution that included Genentech or any of its Affiliates or Sublicensees, (b) has received Regulatory Approval in such jurisdiction for at least one of the same Indications as such Licensed Product as a "generic drug," "generic medicinal product," "bioequivalent" or similar designation of interchangeability by the applicable Regulatory Authority in such jurisdiction pursuant to an expedited, abbreviated or bibliographic approval process in accordance with the then-current rules and regulations in such jurisdiction, where such approval referred to or relied on (A) the approved NDA for such Licensed Product held by Genentech, its Affiliate or a Sublicensee in such

jurisdiction or (B) the data contained or incorporated by reference in such approved NDA for such Licensed Product in such jurisdiction.

1.119 "**Hit**" has the meaning set forth in Section 2.3.1(a).

1.120 "**Hit Success Criteria**" means the criteria [***] applied during the Hit Evaluation Phase to determine whether one (1) or more Bicycle Constructs directed to a given Collaboration Target(s) have met the proof of principle threshold.

1.121 "**Hit Validation Completion Date**" has the meaning as set forth in Section 3.2.4.

1.122 "**Hit Validation Phase**" has the meaning set forth in Section 2.3.1(b).

1.123 "**IND**" means an application filed with a Regulatory Authority for authorization to commence Clinical Studies, including (a) an Investigational New Drug Application as defined in the FFDCA or any successor application or procedure filed with the FDA, (b) any equivalent thereof in other countries or regulatory jurisdictions, (e.g., a Clinical Trial Application (CTA) in the European Union) and (c) all supplements, amendments, variations, extensions and renewals thereof that may be filed with respect to the foregoing.

1.124 "**Indemnification Claim Notice**" has the meaning set forth in Section 13.3.

1.125 "**Indemnified Party**" has the meaning set forth in Section 13.3.

1.126 "**Indemnitee**" has the meaning set forth in Section 13.3.

1.127 "**Indication**" means each separate and distinct disease, disorder, illness, health condition, or interruption, cessation or disruption of a bodily function, system, tissue type or organ, for which Regulatory Approval is required. For clarity, [***].

1.128 "**Initial Collaboration Targets**" means the Modulator Targets set forth on Schedule 1.128.

1.129 "**Initial Discovery Research Plan**" has the meaning set forth in Section 2.2.

1.130 "**Initial Reversion Package**" has the meaning set forth in Section 14.6.1(b).

1.131 "**Initial Reversion Package Period**" has the meaning set forth in Section 14.6.1(b).

1.132 "**Initial Substitution Period**" has the meaning set forth in Section 3.2.1.

1.133 "**Intellectual Property**" has the meaning set forth in Section 14.5.1.

1.134 "**Intermediate Substitution Fee**" has the meaning set forth in Section 3.2.4.

1.135 "**Internal Development Program**" means a bona fide internal program of BicycleTx, pursuant to which BicycleTx is conducting research, development and/or commercialization activities in connection with Bicycles or Bicycle Constructs directed to a [***] Target [***].

1.136 "**Invention**" means any invention, process, method, utility, formulation, composition of matter, article of manufacture, material, creation, discovery, development, or finding, or any improvement thereof, whether or not patentable, including all Intellectual Property rights therein.

1.137 "**Inventory**" means, at the applicable date, all then-existing clinical and non-clinical grade drug product, active pharmaceutical ingredient, intermediates and raw materials for Compounds in the possession or control of Bicycle, as well as any other existing materials (such as Compound reference standards and retention samples), drug delivery systems and packaging for the manufacture or testing of such Compounds and associated Licensed Products.

1.138 "**Joint Collaboration Invention**" has the meaning set forth in Section 1.45.

1.139 "**Joint Collaboration Know-How**" means all Collaboration Know-How that is generated by or on behalf of both Parties or their Affiliates (including any such Know-How developed with a Third Party), including all Know-How in Joint Collaboration Inventions.

1.140 "**Joint Collaboration Patents**" means all Patents that Cover Joint Collaboration Inventions.

1.141 "**JRC**" has the meaning set forth in Section 4.1.1.

1.142 "**Know-How**" means all commercial, technical, scientific, and other know-how and information, Inventions, discoveries, trade secrets, knowledge, technology, methods, processes, practices, formulae, amino acid sequences, nucleotide sequences, instructions, skills, techniques, procedures, ideas, designs, drawings, computer programs, specifications, data and results (including biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, preclinical, clinical, safety, manufacturing and quality control data (including regulatory data, study designs, and protocols), reagents and materials (including assays and compounds)in all cases, whether or not confidential, proprietary, or patentable, in written, electronic, or any other form now known or hereafter developed, but expressly excluding all Patents.

1.143 "**Lead Discovery Construct**" has the meaning set forth in Section 2.3.1(d).

1.144 "**Lead Generation Phase**" has the meaning set forth in Section 2.3.1(c).

1.145 "**Lead Validation Phase**" has the meaning set forth in Section 2.3.1(d).

1.146 "**LIBOR**" means the London Interbank Offered Rate for deposits in United States Dollars having a maturity of one (1) month published by the British Bankers' Association, as adjusted from time to time on the first London business day of each month.

1.147 "**Licensed Product**" means any product, including any Combination Product, comprising or containing a Compound, in any and all forms, presentations, delivery systems, dosage forms and strengths, and formulations.

1.148 "**Losses**" has the meaning set forth in Section 13.1.

1.149 "**LSR Go**" means [***] approval of a Bicycle Construct to begin the Lead Validation Phase [***].

1.150 "**LSR Go Criteria**" means, on a Collaboration Program-by-Collaboration Program basis, the criteria [***] to be achieved by a Discovery Construct in such Collaboration Program at the time of delivery of the LSR Go Data Package. The LSR Go Criteria for the Initial Collaboration Targets as of the Effective Date are set forth on Schedule 1.150.

1.151 "**LSR Go Data Package**" has the meaning set forth in Section 2.5.1(a).

1.152 "**LSR Go Data Package Acceptance Date**" has the meaning set forth in Section 2.5.1(d).

1.153 "**LSR Go Notice**" has the meaning set forth in Section 2.5.1(d).

1.154 "**LSR Go Review Period**" has the meaning set forth in Section 2.5.1(d).

1.155 "**LSR Rejected Program**" has the meaning set forth in Section 2.5.1(e).

1.156 "**MAA**" has the meaning set forth in Section 1.73.

1.157 "**Major Market**" means [***]. If, for a given Licensed Product, [***] "Major Market" shall also mean [***] for such Licensed Product. If [***] unless and until a [***] or between [***] under this Agreement), in each case for such Licensed Product.

1.158 "**Manufacture**", "**Manufactured**" and "**Manufacturing**" means all activities related to the synthesis, making, production, processing, purifying, formulating, filling, finishing, packaging, labeling, shipping, and holding of a Compound, any Licensed Product, or any intermediate thereof, including process development, process qualification and validation, scale-up, pre-clinical, clinical and commercial production and analytic development, product characterization, stability testing, quality assurance, and quality control.

1.159 "**Material Proposed Terms**" has the meaning set forth in Section 14.6.2(d).

1.160 "**Method of Use**" has the meaning set forth in Section 1.203.

1.161 "**Modified Compound**" has the meaning set forth in Section 5.2.

1.162 "**Modulator Target**" means any Target that, when activated, induces or is expected to induce an immuno-modulatory response in a patient.

1.163 "**MTA**" has the meaning set forth in Section 2.4.1.

1.164 "**NDA**" means a "**New Drug Application**", as defined in the FFDCA, as amended, and applicable regulations promulgated thereunder by the FDA and all amendments and supplements thereto filed with the FDA, or the equivalent application filed with any Regulatory Authority, including all documents, data, and other information concerning Licensed Products, which are necessary for gaining Regulatory Approval to market and sell Licensed Product in the relevant jurisdiction.

1.165 "**Negotiation Period**" has the meaning set forth in Section 14.6.1(d).

1.166 "**Net Sales**" means, with respect to a Licensed Product in a particular period, the amount calculated by subtracting from the Sales of such Licensed Product for such period: (i) a lump sum deduction of [***] of Sales in lieu of those deductions that are not accounted for on a Licensed Product-by-Licensed Product basis (e.g., freight, postage charges, transportation insurance, packing materials for dispatch of goods, custom duties); (ii) uncollectible amounts accrued during such period on such Sales and not already taken as a gross-to-net deduction in accordance with the then currently used IFRS in the calculation of Sales of such Licensed Product for such period; (iii) credit card fees (including, if applicable, processing fees) accrued during such period on such Sales and not already taken as a gross-to-net deduction in accordance with the then currently used IFRS in the calculation of Sales of such Licensed Product for such period; and (iv) government mandated fees and taxes (but excluding taxes based on the income of the selling party) and other government charges accrued during such period on such Sales not already taken as a gross-to-net deduction in accordance with the then currently used IFRS in the calculation of Sales of such Licensed Product for such period, including, for example, any fees, taxes or other charges that become due in connection with any healthcare reform, change in government pricing or discounting schemes, or other action of a government or regulatory body. For clarity, no deductions taken in calculating Sales under Section 1.204 may be taken a second time in calculating Net Sales.

For purposes of calculating Net Sales, all Net Sales shall be converted into Dollars in accordance with Section 8.9.

If Genentech or its Affiliates intend to sell a Combination Product in any country or other jurisdiction then the Parties shall [***]

If the Parties' Alliance Managers and Senior Officers are unable to agree on [***] of such referral, then [***] shall be determined by the following procedure: [***] each Party may present at the meeting. The [***] on both Parties. The Parties will [***] of the Expert Committee. Unless otherwise agreed to by the Parties, the [***] may not decide on issues outside the scope mandated under terms of this Agreement.

1.167 "**Nominated Target**" has the meaning set forth in Section 3.1.3.

1.168 "**Non-Breaching Party**" has the meaning set forth in Section 14.3.1.

1.169 "**Non-Compound Active Agent**" has the meaning set forth in Section 1.50.

1.170 "**Option Period**" has the meaning set forth in Section 14.6.1(c).

1.171 "**Party**" and "**Parties**" has the meaning set forth in the preamble hereto.

1.172 "**Patents**" means (a) all national, regional and international patents and patent applications, including provisional patent applications, (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from either of these, including divisionals, continuations, continuations-in-part, provisionals, converted provisionals and continued prosecution applications, (c) any and all patents that have issued or in the future issue from the foregoing patent applications ((a) and (b)), including utility models, petty patents and design patents and certificates of invention, (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any pediatric exclusivity and other such exclusivities that are attached to patents, patent term extensions, supplementary protection certificates and the like) of the foregoing patents or patent applications ((a), (b), and (c)), and (e) any similar rights, including so-called pipeline protection or any importation, revalidation, confirmation or introduction patent or registration patent or patent of additions to any of such foregoing patent applications and patents.

1.173 "**Person**" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department or agency of a government.

1.174 "**Phase II Clinical Trial**" means a Clinical Trial in any country that would satisfy the requirements of 21 C.F.R. § 312.21(b).

1.175 "**Phase III Clinical Trial**" means a Clinical Trial in any country that would satisfy the requirements of 21 C.F.R. § 312.21(c).

1.176 "**Pivotal Clinical Trial**" means either (a) a Clinical Trial the principal purpose of which is to demonstrate clinically and statistically the efficacy and safety of a Licensed Product for one or more Indications in order to obtain Regulatory Approval of such Licensed Product for such Indication(s), as further defined in 21 C.F.R. §312.21 or (b) a Clinical Trial of a Licensed Product on a sufficient number of subjects that, prior to commencement of such trial, satisfies both of the following ((i) and (ii)): (i) such trial is designed to establish that such Licensed Product has an acceptable safety and efficacy profile for its intended use, and to determine warnings, precautions, and adverse reactions that are associated with such Licensed Product in the dosage range to be prescribed, which trial is intended to support Regulatory Approval of such Licensed Product; and (ii) such trial is a registration trial sufficient to support the filing of a Drug Approval Application for such Licensed Product in the U.S., Japan, or a European Major Market, as evidenced by (A) an agreement with or statement from the FDA or the EMA on a 'Special Protocol Assessment' or equivalent, or (B) other guidance or minutes issued by the FDA or EMA, for such registration trial.

1.177 "**Platform Invention**" means an Invention that (a) is generated in the performance of activities under this Agreement, (b) relates to the BicycleTx Platform or any component of the BicycleTx Platform, and (c) [***] a Compound or Licensed Product.

1.178 "**PMDA**" means Japan's Pharmaceuticals and Medical Devices Agency and any successor agency(ies) or authority having substantially the same function.

1.179 "**POP Achievement**" has the meaning set forth in Section 2.3.1(b).

1.180 "**POP Achievement Date**" means the date of the JRC meeting at which POP Achievement is confirmed, [***], or the date that the Parties mutually agree in writing that POP Achievement has occurred, if earlier.

1.181 "**Prior NDA**" has the meaning set forth in Section 1.54.

1.182 "**Product Infringement**" has the meaning set forth in Section 9.5.1(a).

1.183 "**Product Labeling**" means, with respect to a Licensed Product in a country or other jurisdiction in the Territory, (a) the Regulatory Authority-approved full prescribing information for such Licensed Product for such country or other jurisdiction, including any required patient information, and (b) all labels and other written, printed, or graphic matter upon a container, wrapper, or any package insert utilized with or for such Licensed Product in such country or other jurisdiction.

1.184 "**Product Invention**" means, on a Compound-by-Compound and Licensed Product-by-Licensed Product basis, a Collaboration Invention that [***] relates to a Compound, Discovery Construct, Development Candidate and/or a Licensed Product.

1.185 "**Product Know-How**" means, on a Compound-by-Compound and Licensed Product-by-Licensed Product basis, all Collaboration Know-How that is [***] related to such Compound and/or Licensed Product, including all Know-How in Product Inventions.

1.186 "**Product Patents**" means (a) all Patents that Cover any Product Invention and (b) the Patents deemed Product Patents pursuant to Section 9.4.1(b).

1.187 "**Product Trademarks**" means the Trademark(s) to be used by Genentech or its Affiliates or its or their respective Sublicensees for the Development or Commercialization of Licensed Products in the Territory and any registrations thereof or any pending applications relating thereto in the Territory (excluding, in any event, any trademarks, service marks, names or logos that include any corporate name or logo of the Parties or their Affiliates).

1.188 "**Proposed Target**" has the meaning set forth in Section 3.1.2.

1.189 "**Proposed Terms**" has the meaning set forth in Section 14.6.2(d).

1.190 "**Publishing Notice**" has the meaning set forth in Section 11.5.2.

1.191 "**Publishing Party**" has the meaning set forth in Section 11.5.2.

1.192 "**Redacted Agreement**" shall have the meaning set forth in Section 11.2.2.

1.193 "**Regulatory Approval**" means, with respect to a country or other jurisdiction in the Territory, all approvals (including Drug Approval Applications), licenses, registrations, or authorizations of any Regulatory Authority necessary to Commercialize a Discovery Construct or Licensed Product in such country or other jurisdiction, and including pricing or reimbursement approval in such country or other jurisdiction solely where such pricing and reimbursement approval is legally required for the sale of such Licensed Product.

1.194 "**Regulatory Authority**" means any applicable supra-national, federal, national, regional, state, provincial, or local governmental or regulatory authority, agency, department, bureau, commission, council, or other entities (e.g., the FDA, EMA and PMDA) regulating or otherwise exercising authority with respect to activities contemplated in this Agreement, including the Exploitation of the Discovery Constructs or Licensed Products in the Territory.

1.195 "**Regulatory Documentation**" means all (a) applications (including all INDs and Drug Approval Applications), registrations, licenses, authorizations, and approvals (including Regulatory Approvals), (b) correspondence and reports submitted to or received from Regulatory Authorities (including minutes and official contact reports relating to any communications with any Regulatory Authority) and all supporting documents with respect thereto, including all regulatory drug lists, advertising and promotion documents, adverse event files, and complaint files, and (c) Clinical Data and data contained or relied upon in any of the foregoing, in each case ((a), (b), and (c)) to the extent relating to a Discovery Construct or Licensed Product.

1.196 "**Relative Commercial Value**" has the meaning set forth in Section 1.166.

1.197 "**Research Term**" means, on a Collaboration Program-by-Collaboration Program basis, the period of time in which the Discovery Research Plan for such Collaboration Program shall be conducted, (a) commencing, as the case may be, [***] and (b) ending upon the earlier of [***].

1.198 "**Reversion Agreement**" has the meaning set forth in Section 14.6.1(d).

1.199 "**Reversion Packages**" has the meaning set forth in Section 14.6.1(b).

1.200 "**Reversion Proceeding**" shall have the meaning set forth in Section 14.6.2.

1.201 "**Reversion Rights**" has the meaning set forth in Section 14.6.1(c).

1.202 "**Reversion Terms**" has the meaning set forth in Section 14.6.1(d).

1.203 "**Royalty Term**" means, with respect to each Licensed Product and each country or other jurisdiction in the Territory, the period beginning on the date of the First Commercial Sale of such Licensed Product in such country or other jurisdiction, and ending on the latest to occur of (a) the tenth (10^{th}) anniversary of the First Commercial Sale of such Licensed Product in such country or other jurisdiction or (b) the expiration date of the last Valid Claim of any Joint Collaboration Patent or any BicycleTx Patent that Covers [***].

1.204 "**Sales**" means, for a Licensed Product in a particular period, the sum of the amounts calculated pursuant to Sections 1.204.1 and 1.204.2:

1.204.1 The amount stated in the Roche Holding AG "Sales" line (or its equivalent, regardless of description) of its externally published audited consolidated financial statements with respect to such Licensed Product for such period (excluding sales to any Sublicensees that are not Affiliates of Genentech) (or, if audited financial statements are not prepared for such period, the corresponding amount as reasonably determined for unaudited financial statements for such period, which amounts, and associated royalties and reports, shall be reconciled with an audited financial statement at such time as an audited financial statement for a period covering such period is prepared). This amount reflects the gross invoice price at which such Licensed Product was sold or otherwise disposed of (other than for use as clinical supplies or free samples) by Genentech and its Affiliates to such Third Parties (excluding sales to any Sublicensees that are not Affiliates of Genentech) in such period reduced by gross-to-net deductions, if not previously deducted from such invoiced amount, taken in accordance with the then currently used IFRS, to the extent any such gross-to net deductions are actually allowed. By way of example, the gross-to-net deductions taken in accordance with IFRS as of the Effective Date and actually taken and consistently applied across all of Genentech's products (including Licensed Products) include the following:

[***]

[***]

For purposes of clarity, sales by Genentech and its Affiliates to any Sublicensee shall be excluded from the calculation of "Sales" so long as the subsequent resale by a Sublicensee to a Third Party shall be included in the calculation of "Sales" as set forth in Section 1.204.2

1.204.2 For Sublicensees that are not Genentech Affiliates (and excluding compulsory sublicensees, which shall not be considered Sublicensees as that term is used throughout this Agreement), the sales amounts reported to Genentech and its Affiliates in accordance with the applicable sublicense agreement contractual terms and such Sublicensee's then-currently used Accounting Standards consistently applied across all of such Sublicensee's products, so long as such reported amounts are not materially less than what the calculation of Sales would have been if such sales had been made by Genentech and calculated in accordance with Section 1.204.1. For the purpose of clarity, any sales reported to Genentech in accordance with a compulsory sublicense agreement (i.e., a sublicense granted to a Third Party through the order, decree, or grant of a governmental authority having competent jurisdiction authorizing such Third Party to make, use, sell, offer for sale, import and export a Licensed Product in such jurisdiction) shall be excluded from the calculation of "Sales".

1.205 "**Secondary Reversion Package**" has the meaning set forth in Section 14.6.1(b).

1.206 "**Secondary Reversion Package Period**" has the meaning set forth in Section 14.6.1(b).

1.207 "**Segregate**" means with respect to a Segregation Product, to segregate the development and commercialization activities relating to such Segregation Product in the Field from Development and Commercialization activities with respect to Compounds and Licensed Products under this Agreement, including to ensure that: (a) [***]; and (b) [***].

1.208 "**Segregation Product**" means any pharmaceutical or biologic product, process, service or therapy that is directed to any Modulator Target that is the subject of any Collaboration Program hereunder, for any Indication.

1.209 "**Senior Officer**" means, with respect to BicycleTx, its [***] or his/her designee, and with respect to Genentech, it [***] or his/her designee.

1.210 "**Sublicensee**" means a Person, other than an Affiliate or a Distributor, that is granted a sublicense by Genentech under the grants in Section 7.1 as provided in Section 7.4.

1.211 "**Substitute Target**" has the meaning set forth in Section 3.2.1.

1.212 "**Target**" means [***] or similar information, such as its [***]. Such Target shall be deemed to include (a) [***]

[***]; and (b) [***].

1.213 "**Target Acceptance Date**" has the meaning set forth in Section 3.1.3.

1.214 "**Target Availability Notice**" has the meaning set forth in Section 3.1.3.

1.215 "**Target Exclusivity Period**" has the meaning set forth in Section 7.8.2.

1.216 "**Targeting Arm**" means a Bicycle directed to an Antigen Target.

1.217 "**Targeting Arm Criteria**" has the meaning set forth in Section 2.3.2(j).

1.218 "**Targeting Arm Data Package**" has the meaning set forth in Section 2.3.2(j).

1.219 "**Targeting Arm Data Package Acceptance Date**" has the meaning set forth in Section 2.3.2(j).

1.220 "**Targeting Arm Notice**" has the meaning set forth in Section 2.3.2(k).

1.221 "**Targeting Arm Review Period**" has the meaning set forth in Section 2.3.2(k).

1.222 "**Target Nomination Fee**" has the meaning set forth in Section 3.1.1(e).

1.223 "**Target Nomination Notice**" has the meaning set forth in Section 3.1.3.

1.224 "**Target Substitution**" has the meaning set forth in Section 3.2.

1.225 "**Term**" has the meaning set forth in Section 14.1.

1.226 "**Terminated Asset**" means, on a Collaboration Program-by-Collaboration Program basis, with respect to a Collaboration Program that is terminated by either Party under ARTICLE 14 following Genentech's delivery of a Dev Go Notice, each Compound, Discovery Construct, Development Candidate and Licensed Product directed to the Terminated Target that is the subject of such Collaboration Program.

1.227 "**Terminated Target**" means a Collaboration Target that is (a) the subject of a Collaboration Program that has been terminated for any reason pursuant to ARTICLE 14, (b) the subject of a Collaboration Program for which Genentech has elected not to deliver (or otherwise did not timely deliver) a LSR Go Notice or a Dev Go Notice, as applicable, or (c) no longer included within a Collaboration Program following a Target Substitution.

1.228 "**Terminated Territory**" means (a) each Major Market with respect to which this Agreement is terminated by BicycleTx pursuant to Section 14.3.3, (b) each country with respect to which the Agreement is terminated by Genentech pursuant to Section 14.2 or 14.3.1, or (c) if this Agreement is terminated in its entirety, the entire Territory.

1.229 "**Territory**" means the entire world.

1.230 "**Third Party**" means any Person other than BicycleTx, Genentech and their respective Affiliates.

1.231 "**Third Party Claims**" has the meaning set forth in Section 13.1.

1.232 "**Third Party Negotiations**" means ongoing negotiations with a Third Party on a research plan and/or financial or other deal terms, [***].

1.233 "**Third Party Provider**" has the meaning set forth in Section 5.5.

1.234 "**Trademark**" means any word, name, symbol, color, scent, design, designation or device or any combination thereof that functions as a source identifier, including any trademark, trade dress, brand mark, service mark, trade name, brand name, logo, business symbol or domain name, whether or not registered.

1.235 "**Unavailable Target(s)**" means any [***] Target that is not available for nomination as a Collaboration Target by Genentech under this Agreement because such [***] Target is (a) the subject of an active, executed written agreement with a Third Party granting a license, or other rights with respect to Bicycle Constructs or products intended for use against such [***] Targets that would prevent BicycleTx from granting the rights to Genentech set forth in this Agreement, (b) the subject of an Internal Development Program, or (c) [***] such [***] Target.

1.236 "**Unblocking License**" means:

(a) a non-exclusive, royalty-free, sublicenseable, worldwide license under [***];

(b) solely in the case of a termination of this Agreement under ARTICLE 14, a [***] Bicycle Construct directed to a Terminated Target; and

(c) an [***] license under Genentech's interest in and to all Joint Collaboration Patents (collectively, the Patents in (a) through (c), the "**Unblocking Patents**"),

in each case of (a) through (c) for the sole purpose of, and solely to the extent necessary to Exploit Bicycle Constructs directed to the applicable Terminated Target, provided that the licenses set forth above shall expressly exclude any grant of rights to (i) any Non-Compound Active Agents that are Covered by such Unblocking Patents and (ii) [***]. For clarity, Genentech [***].

1.237 "**Unblocking Patents**" has the meaning set forth in Section 1.236.

1.238 "**United States**" or "**U.S.**" means the United States of America and its territories and possessions (including the District of Columbia and Puerto Rico).

1.239 "**United States – United Kingdom Income Tax Convention**" means the Convention between the government of the United States of America and the government of the United Kingdom of Great Britain and Northern Ireland for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital Gains.

1.240 "**Valid Claim**" means a claim of any issued and unexpired Patent whose validity, enforceability, or patentability has not been rendered invalid by any of the following: (a) irretrievable lapse, abandonment, revocation, dedication to the public, or disclaimer; or (b) a holding, finding, or decision of invalidity, unenforceability, or non-patentability by a court, governmental agency, national or regional patent office, or other appropriate body that has competent jurisdiction, such holding, finding, or decision being final and unappealable or unappealed within the time allowed for appeal.

1.241 "**Working Group**" has the meaning set forth in Section 4.8.

ARTICLE 2
DISCOVERY COLLABORATION AND ACTIVITIES

2.1 Collaboration Overview. For each Collaboration Target, BicycleTx shall perform Discovery Research Activities in connection with Bicycle Constructs directed to such Collaboration Target with or without a Targeting Arm (each, a "**Collaboration Program**") pursuant to a Discovery Research Plan. The Discovery Research Activities are aimed at generating Bicycle Constructs that are directed to the applicable Collaboration Target and suitable to progress through Genentech's LSR Go and Dev Go, in order to select and advance a Development Candidate into further pre-clinical and clinical Development and Commercialization as a Licensed Product.

2.2 Discovery Research Plan. The Discovery Research Plan for the Initial Collaboration Targets as of the Effective Date (the "**Initial Discovery Research Plan**") is as attached hereto as Schedule 1.69. Subject to ARTICLE 4, the Parties may amend the Initial Discovery Research Plan or any subsequent Discovery Research Plan for subsequent Collaboration Targets upon agreement of the JRC.

2.3 Phases of the Collaboration.

2.3.1 Modulator Targets. In general, for each Modulator Target that is the subject of a Collaboration Program, the Discovery Research Activities under the Discovery Research Plan will be divided into the following stages (each, a "**Discovery Phase**"):

(a) BicycleTx will perform an initial evaluation and feasibility screen to generate Bicycles suitable for binding the specified Modulator Target, which screen will be focused on generating a series of alternative Bicycle Constructs that are directed to and capable of binding the applicable Modulator Target, and are considered suitable for further evaluation as potential Discovery Constructs (each such Bicycle Construct, a "**Hit**" and such discovery phase, the "**Evaluation Phase**"). BicycleTx will notify Genentech in writing (which may be through the JRC) promptly following completion of the Evaluation Phase for each Modulator Target, which shall include details of the Hits

identified in such Evaluation Phase (the "**Evaluation Completion Notice**") in order for Genentech to determine whether or not it wishes to exercise its substitution right under Section 3.2.

(b) If the Evaluation Phase results in one (1) or more Hits, BicycleTx will perform a full validation screen of the identified Hits, initially evaluating such Hits against the Hit Success Criteria (such phase, the "**Hit Validation Phase**"). The Hit Success Criteria for the Initial Collaboration Targets are set forth in Schedule 1.120. The Hit Success Criteria for additional Modulator Targets shall be substantially similar in form and content to the criteria set forth in Schedule 1.120, [***]. Bicycle Constructs that achieve the Hit Success Criteria will be deemed to have met the proof-of-principle threshold (the achievement of proof-of-principle by one or more Bicycle Constructs, the "**POP Achievement**" for the applicable Modulator Target). Bicycle Constructs that reach POP Achievement will be progressed by BicycleTx through the remainder of the validation screens and completion of the Hit Validation Phase. Bicycle Constructs that successfully complete the Hit Validation Phase will be deemed "**Discovery Constructs**".

(c) Following completion of the Hit Validation Phase, BicycleTx will perform characterization, prioritization and optimization of each such Discovery Construct in accordance with the Discovery Research Plan (the "**Lead Generation Phase**") to identify one or more lead Discovery Constructs [***]. Following completion of the Lead Generation Phase for Discovery Constructs directed to a given Modulator Target, BicycleTx will submit to Genentech the LSR Go Data Package in accordance with Section 2.5.1(a).

(d) If Genentech determines, in its sole discretion, to progress Discovery Research Activities beyond LSR Go, the Parties will select one or more lead Discovery Constructs (a "**Lead Discovery Construct**") to be the subject of initial pre-clinical Development by BicycleTx, [***], in each case as further set forth in the Discovery Research Plan (such phase, the "**Lead Validation Phase**"). The Lead Validation Phase may be performed on (i) a Discovery Construct directed solely to a Modulator Target, or (ii) a Discovery Construct directed to a Modulator Target that also incorporates a Targeting Arm ([***]). Following completion of the Lead Validation Phase for one or more Lead Discovery Constructs directed to a given Collaboration Target, BicycleTx will submit to Genentech the Dev Go Data Package in accordance with Section 2.5.2(a) in order for Genentech to determine whether it wishes to progress such Lead Discovery Construct into further pre-clinical Development, [***]. Any Discovery Construct selected by Genentech to progress into further pre-clinical Development following the Lead Validation Phase, including any Modified Compound will be designated a "**Development Candidate**".

2.3.2 Antigen Targets; Targeting Arms.

(a) Subject to Genentech's substitution rights under Section 3.2, Genentech has the right to select, in its sole discretion, a total of up to four (4) Antigen Targets as Collaboration Targets for Targeting Arms under this Agreement (i.e., one (1) Antigen Target for each Collaboration Program), as set forth in the remainder of this Section 2.3.2.

(b) BicycleTx will evaluate and utilize [***] Targeting Arms in each Collaboration Program according to the Discovery Research Plan. If [***] Targeting Arm is incorporated into a Licensed Product, then Section 8.5.2 applies.

(c) In addition, Genentech may request that BicycleTx evaluate and utilize other Targeting Arms in Collaboration Programs. If such request is for a BicycleTx Future Independent Targeting Arm, then, if the applicable Targeting Arm is also listed in Part 1 of Schedule 2.3.2 ("**Genentech Targeting Arms of Interest**"), then BicycleTx will evaluate such a Genentech Targeting Arm of Interest according to the applicable Discovery Research Plan, and [***]. If such requested Targeting Arm is not listed as a Genentech Targeting Arm of Interest, but is a BicycleTx Future Independent Targeting Arm, such BicycleTx Future Independent Targeting Arm shall be subject to confirmation of the availability of the applicable Antigen Target pursuant to Section 3.1.3 or Section 3.1.5, as applicable. For clarity, [***] upon selection of the applicable Antigen Target, if available, and BicycleTx will evaluate such other BicycleTx Future Independent Targeting Arm according to the applicable Discovery Research Plan, provided that [***].

(d) Genentech may request that BicycleTx evaluate and utilize Targeting Arms directed to Antigen Targets selected by Genentech and which are not targeted by any Existing Targeting Arm or BicycleTx Future Independent Targeting Arm pursuant to Section 2.3.2(c) ("**Genentech Antigen Target**"). Genentech shall make an inquiry regarding the availability of such Genentech Antigen Target pursuant to Section 3.1.3 or Section 3.1.5, as applicable. For clarity, [***] upon selection of such Genentech Antigen Target, if available, and BicycleTx will evaluate such other BicycleTx Future Independent Targeting Arm according to the applicable Discovery Research Plan, provided that the generation of Targeting Arms directed to Genentech Antigen Targets ("**Genentech Targeting Arms**") shall be subject to the payments set forth in Section 8.2.2.

(e) BicycleTx may [***]. If BicycleTx desires to [***].

(f) Genentech may [***]. If Genentech [***].

(g) Without limiting the generality of the foregoing Sections 2.3.2(e) and 2.3.2(f), both Parties may [***]

[***] basis, without [***]. At Genentech's request, BicycleTx shall [***] that exists as of the Targeting Arm Data Package Acceptance Date for the [***].

(h) Notwithstanding the last sentence of Section 2.3.2(f), from the Effective Date until [***] (the "[***] **Option Period**"), Genentech has the option to [***] Targeting Arm ("[***] **Products**") outside this Agreement (the "[***] **Option**", and the associated license, the "[***] **License**"). For clarity, the right under the [***] License [***], and does not include the right to [***] basis. Genentech may exercise the [***] Option by providing written notice to BicycleTx ("[***] **Option Notice**") any time within the [***] Option Period. Following BicycleTx's receipt of the [***] Option Notice during the [***] Option Period, the Parties shall negotiate in good faith for a period of [***] terms of the [***] License, which shall be [***].

(i) Notwithstanding the last sentence of Section 2.3.2(e), after the earlier of the date of (i) [***] Targeting Arm (and subject to Section 7.8)] and (ii) [***], BicycleTx may [***], provided that BicycleTx notifies Genentech in writing [***] within [***] from Genentech therefor. If BicycleTx [***] a Third Party to use the [***] Targeting Arm, then BicycleTx shall provide Genentech with [***] Genentech of [***] within [***] after receipt of an invoice from Genentech therefor.

(j) The Discovery Research Activities for each such Targeting Arm will proceed through the Evaluation Phase, Hit Validation Phase and Lead Generation Phase in substantially the same manner as for Modulator Targets, with BicycleTx evaluating, validating, and optimizing Targeting Arms directed to such Antigen Target, and evaluating activity of such Targeting Arm in connection with the applicable Discovery Construct in accordance with the amended Discovery Research Plan. Following the completion of the Lead Generation Phase for a Targeting Arm, BicycleTx will provide Genentech, through the JRC, with a data package of information and data relating to the combination of such Targeting Arm with the selected Discovery Construct and confirmation that the Targeting Arm has met the criteria [***], which shall be [***] Targeting Arm, [***] (the "**Targeting Arm Criteria**", such Targeting Arm Criteria applicable for the [***] Targeting Arm being set forth in Part 3 of Schedule 2.3.2, and each such data package, a "**Targeting Arm Data Package**"). During the [***] period immediately following delivery of a Targeting Arm Data Package, or such longer period as the Parties may agree in writing, Genentech may (i) identify data or

information that Genentech considers is missing from such Targeting Arm Data Package, and request in writing that BicycleTx provides such missing information or data, and (ii) make reasonable inquiries of BicycleTx for further clarification and information in connection with the data and information included in such Targeting Arm Data Package, or the achievement of the Targeting Arm Criteria. With respect to (A) any data or information identified as missing from such Targeting Arm Data Package, BicycleTx shall update such Targeting Arm Data Package to include any such missing information and shall deliver a revised Targeting Arm Data Package [***] after the receipt of such request from Genentech; and (B) Genentech's other inquiries, BicycleTx will [***]; provided that in the case of (B), BicycleTx shall not be required to perform any additional assays or analyses or generate any additional data in connection with such requests. The Targeting Arm Data Package shall be deemed complete upon the later of (1) the delivery to Genentech of a complete Targeting Arm Data Package containing the information identified by Genentech in subclause (i) and confirmation by the JRC that the Targeting Arm Criteria have been met, or (2) the expiration of such [***] review period (the "**Targeting Arm Data Package Acceptance Date**").

(k) Genentech shall determine, in its sole discretion, within [***] following the Targeting Arm Data Package Acceptance Date (the "**Targeting Arm Review Period**"), whether it wishes to progress the applicable Discovery Construct into initial pre-clinical Development activities with the incorporation of the evaluated Targeting Arm. Genentech shall notify BicycleTx in writing of its decision (the "**Targeting Arm Notice**") prior to the expiration of the Targeting Arm Review Period, and if such decision is in the affirmative BicycleTx shall thereafter progress such Discovery Construct (including such Targeting Arm) into the Lead Validation Phase, and the applicable Collaboration Program shall be deemed to include such Targeting Arm and the applicable Antigen Target to which it is directed.

2.4 Discovery Research Activities.

2.4.1 For each Collaboration Program (including any Substitute Target or activities with respect to a Targeting Arm), BicycleTx shall carry out the Discovery Research Activities for each Discovery Phase. BicycleTx shall perform the Discovery Research Activities in good scientific manner, in accordance with this Agreement, and in compliance with all Applicable Law, and shall use diligent efforts to complete the activities for each Collaboration Target set forth in the Discovery Research Plan during the applicable Research Term. Through the JRC, Genentech shall provide reasonable intellectual assistance requested by BicycleTx in connection with its performance of the Discovery Research Activities. Genentech, at is sole discretion, may also agree to perform certain Discovery Research Activities pursuant to mutual agreement of the JRC. If applicable, Genentech shall perform all such Discovery Research Activities in good scientific manner in accordance this Agreement, and in compliance with all Applicable Law. BicycleTx may agree from time to time to transfer materials, including any Bicycle Constructs or Discovery Constructs to Genentech, to enable Genentech to perform certain Discovery Research Activities. BicycleTx's agreement for any such transfer shall not be unreasonably withheld, conditioned or delayed and shall be performed under the terms of a material transfer agreement (the "**MTA**"), which MTA shall provide that (a) such materials may only be used in connection with the Discovery Research Activities Genentech has agreed to perform, during the period set forth in such MTA, and (b) no modification or reverse engineering of any materials by or on behalf of Genentech will be permitted, except to the extent expressly set forth in such MTA. The Parties shall negotiate in good faith and agree upon the form of such MTA [***].

2.4.2 If, with respect to a given Collaboration Program, the JRC concludes that the Discovery Research Activities for such Collaboration Program will not be completed by the end of the applicable Research Term as defined in Section 1.197(b)(i), then the Parties may via the JRC mutually agree to extend such Research Term for an additional period of time so as to permit the completion of the remaining Discovery Research Activities, and BicycleTx shall [***] (provided that the remaining [***], provided that [***] in connection with such extension [***], then [***] extension [***]. BicycleTx shall conduct Discovery Research Activities concurrently on up to [***] Collaboration Targets, provided that [***], then the foregoing [***].

2.4.3 Following the completion of the Discovery Research Activities for each Discovery Phase for each Collaboration Program, BicycleTx shall deliver to Genentech, through the JRC, the results and data arising from such Discovery Phase and set forth to be delivered to the JRC in the applicable Discovery Research Plan. In addition, (a) following the completion of the Lead Generation Phase for each Collaboration Program, BicycleTx shall deliver to Genentech the LSR Go Data Package in order for Genentech to determine whether to progress the applicable Collaboration Program into the Lead Validation Phase, as further set forth in Section 2.5.1, and (b) following the completion of the Lead Validation Phase for each Collaboration Program, BicycleTx shall deliver to Genentech the Dev Go Data Package in order for Genentech to determine whether to progress the applicable Collaboration Program into further pre-clinical Development activities, as further set forth in Section 2.5.2.

2.5 Discovery Progression Decision Points.

2.5.1 LSR Go.

(a) Promptly following the completion of the Lead Generation Phase for each Collaboration Program, BicycleTx will notify Genentech and provide the JRC with a draft data package that BicycleTx intends to submit in order for Genentech to make a decision regarding LSR Go, which data package will include the following information and data relating to all Discovery Constructs generated under such Collaboration Program that meet the Discovery Construct Threshold: (i) [***] for inclusion in such data package, (ii) the results of the testing and analyses performed to characterize and prioritize such Discovery Constructs during the Lead Generation Phase, including the performance against and confirmation (or otherwise) of achievement of the LSR Go Criteria, (iii) BicycleTx's recommendations for selection of a Lead Discovery Construct from those Discovery Constructs that met the Discovery Construct Threshold, and (iv) any results and data generated in the performance of the Hit Validation Phase (to the extent not already provided to Genentech) (each such data package, an "**LSR Go Data Package**").

(b) The Parties will discuss the draft LSR Go Data Package at the applicable JRC meeting, and within [***] following such JRC meeting, Genentech may (i) identify data or information that Genentech reasonably considers is missing from such draft LSR Go Data Package, and

request in writing that BicycleTx provides such missing information or data, and (ii) make reasonable inquiries of BicycleTx for further clarification and information in connection with the data and information included in such draft LSR Go Data Package, and the basis for BicycleTx's analyses or designation of any Lead Discovery Constructs. For clarity, [***]. With respect to any data or information identified as missing from such draft LSR Go Data Package, BicycleTx shall promptly update such draft LSR Go Data Package to include any such missing information or provide responses to Genentech's other inquiries, provided that BicycleTx shall not be required to perform any additional assays or analyses or generate any additional data in connection with such requests. If the Parties agree at the JRC meeting that the draft LSR Go Data Package is complete, or if Genentech makes no requests for additional information under subclause (i) or (ii) within the [***] period following such JRC meeting, then the LSR Go Data Package will be deemed to be in final form, and Section 2.5.1(d) will apply.

(c) If Genentech requests further information in connection with the draft LSR Go Data Package pursuant to Section 2.5.1(b), BicycleTx shall notify Genentech when such information is available and the Parties shall schedule a further meeting of the JRC no later than [***] following such notice to Genentech to consider such revised draft LSR Go Data Package. Unless Genentech identifies, at the time of such JRC meeting, further information that is reasonably required to be included (in which case Section 2.5.1(b) shall apply again to such review and provision of information), the LSR Go Data Package shall be deemed complete at such JRC meeting.

(d) Genentech shall schedule a meeting [***] as soon as practicable following the date of the JRC meeting at which the LSR Go Data Package is deemed final (or expiration of the [***] period for requests for additional information under Section 2.5.1(b), if applicable), and shall notify BicycleTx of the date of such meeting. Genentech may, [***], (i) identify data or information [***] missing from the LSR Go Data Package, and request in writing that BicycleTx provides such missing information or data, and (ii) make reasonable inquiries of BicycleTx for further clarification and information in connection with the data and information included in such LSR Go Data Package, the achievement (or otherwise) of the LSR Go Criteria, and the basis for BicycleTx's analyses or designation of any Lead Discovery Constructs. With respect to any data or information reasonably identified [***] as missing from such LSR Go Data Package, or responses to Genentech's inquiries, BicycleTx shall promptly provide such responses or update such LSR Go Data Package to include any such missing information and shall deliver a revised LSR Go Data Package as soon as reasonably practicable. The LSR Go Data Package shall be deemed complete upon the later of (A) the delivery [***] of a complete LSR Go Data Package containing the additional information requested [***], as confirmed in writing by Genentech, and (B) the expiration of such [***] review period (the "**LSR Go Data Package Acceptance Date**"). Genentech shall determine, in its sole discretion, within [***] following the LSR Go Data Package Acceptance Date (the "**LSR Go Review Period**"), whether the applicable Discovery Constructs have achieved LSR Go and are suitable to advance into initial pre-clinical Development activities. Genentech shall notify BicycleTx in writing of its decision (the "**LSR Go Notice**") prior to the expiration of the LSR Go Review Period, and if such decision is in the affirmative Genentech shall also designate in such LSR Go Notice the one or more Lead Discovery Construct(s) for such Collaboration Target.

(e) On a Collaboration Program-by-Collaboration Program basis, if Genentech does not timely deliver a LSR Go Notice for such Collaboration Program (a "**LSR Rejected Program**"), BicycleTx shall have the right thereafter to conduct research, Development and Commercialization in connection with the Discovery Constructs and Compounds directed to the applicable Terminated Target, and to grant rights to Third Parties to conduct any of the foregoing activities based on the data and information included in the LSR Go Data Package provided to Genentech for such LSR Rejected Program without further obligations to Genentech. Notwithstanding the foregoing, if BicycleTx [***] period following the expiration of the LSR Go Review Period, [***], as follows: (i) BicycleTx shall provide written notice to Genentech within such [***] period of [***] applicable LSR Go Data Package, (ii) Genentech shall have a period of [***] in which to [***] of this Agreement, (iii) Genentech may [***] period, and BicycleTx shall [***], (iv) if Genentech provides such notice, Genentech shall [***] following the date of such notice, [***] such LSR Rejected Program if Genentech [***] for such LSR Rejected Program, and (v) effective upon the date of the [***], (A) such LSR Rejected Program shall once again become a Collaboration Program, (B) all of the terms of this Agreement, including, for clarity, the exclusivity provisions in Section 7.8, shall once again apply to such Collaboration Program.

2.5.2 Dev Go.

(a) Promptly following the completion of the Lead Validation Phase for each Collaboration Program, BicycleTx will notify Genentech and provide the JRC with a draft data package that BicycleTx intends to submit in order for Genentech to make a decision regarding Dev Go, which data package will include the following information and data relating to the Lead Discovery Constructs for such Collaboration Program: (i) [***] for inclusion in such data package, (ii) the results of the testing and analyses performed to characterize and prioritize such Lead Discovery Constructs during the Lead Validation Phase, including the performance against and confirmation (or otherwise) of achievement of the Dev Go Criteria, (iii) the Compounds for such Collaboration Program, (iv) BicycleTx's recommendations for Development Candidate selection, and (v) any results and data generated in the performance of the Lead Validation Phase (to the extent not already provided to Genentech) (each such data package, a "**Dev Go Data Package**").

(b) The Parties will discuss the draft Dev Go Data Package at the applicable JRC meeting, and within [***] following such JRC meeting, Genentech may (i) identify data or information that Genentech reasonably considers is missing from such draft Dev Go Data Package, and request in writing that BicycleTx provides such missing information or data, and (ii) make reasonable inquiries of BicycleTx for further clarification and information in connection with the data and information included in such draft Dev Go Data Package, the achievement or otherwise of the Dev Go Criteria, and the basis for BicycleTx's analyses or designation of any Development Candidates included therein. For clarity,

[***]. With respect to any data or information identified as missing from such draft Dev Go Data Package, BicycleTx shall promptly update such draft Dev Go Data Package to include any such missing information or provide responses to Genentech's other inquiries, provided that BicycleTx shall not be required to perform any additional assays or analyses or generate any additional data in connection with such requests. If the Parties agree at the JRC meeting that the draft Dev Go Data Package is complete, or if Genentech makes no requests for additional information under subclause (i) or (ii) within the [***] period following such JRC meeting, then the Dev Go Data Package will be deemed to be in final form, and Section 2.5.2(d) will apply.

(c) If Genentech requests further information in connection with the draft Dev Go Data Package pursuant to Section 2.5.2(b), BicycleTx shall notify Genentech when such information is available and the Parties shall schedule a further meeting of the JRC no later than [***] following such notice to Genentech to consider such revised draft Dev Go Data Package. Unless Genentech identifies, at the time of such JRC meeting, further information that is reasonably required to be included (in which case Section 2.5.2(b) shall apply again to such review and provision of information), the Dev Go Data Package shall be deemed complete at such JRC meeting.

(d) Genentech shall schedule a meeting [***] as soon as practicable following the date of the JRC meeting at which the Dev Go Data Package is deemed final (or expiration of the [***] period for requests for additional information under Section 2.5.2(b), if applicable), and shall notify BicycleTx of the date of such meeting. Genentech may, [***], (i) identify data or information [***] missing from the Dev Go Data Package, and request in writing that BicycleTx provides such missing information or data, and (ii) make reasonable inquiries of BicycleTx for further clarification and information in connection with the data and information included in such Dev Go Data Package, and the basis for BicycleTx's analyses or designation of any Development Candidates included therein. With respect to any data or information [***] missing from such Dev Go Data Package, or responses to Genentech's inquiries, BicycleTx shall promptly provide such responses or update such Dev Go Data Package to include any such missing information and shall deliver a revised Dev Go Data Package as soon as reasonably practicable. The Dev Go Data Package shall be deemed complete upon the later of (A) the delivery [***] of a complete Dev Go Data Package containing the additional information requested [***], as confirmed in writing by Genentech, and (B) the expiration of such [***] review period (the "**Dev Go Data Package Acceptance Date**"). Genentech shall determine, in its sole discretion, within [***] following the Dev Go Data Package Acceptance Date (the "**Dev Go Review Period**"), whether the applicable Discovery Constructs have achieved Dev Go and are suitable to advance into further pre-clinical Development activities. Genentech shall notify BicycleTx in writing of its decision (the "**Dev Go Notice**") prior to the expiration of the Dev Go Review Period, and if such decision is in the affirmative Genentech shall also designate in such Dev Go Notice one or more Development Candidates for such Collaboration Target.

2.5.3 Termination of Discovery Research Activities for a Collaboration Program. If Genentech determines in its sole discretion at either the LSR Go or Dev Go decision points that it does not wish to pursue further Discovery Research Activities or Development in connection with a given

Collaboration Program, it shall provide written notice to BicycleTx of such decision, and as of and following the date of such notice: (a) BicycleTx's Exclusivity Obligations with respect to the applicable Collaboration Target(s) and Collaboration Program(s) pursuant to Section 7.8 shall terminate, and subject to Genentech's rights under Section 2.5.1(e), such Collaboration Target shall become a Terminated Target, (b) all rights and licenses granted to Genentech by BicycleTx in connection with such Collaboration Program will terminate, except that (i) [***], and (ii) [***] in connection with the Terminated Target. For clarity, if Genentech provides no response in writing to BicycleTx before the expiration of the LSR Go Review Period, or the Dev Go Review Period, as applicable, Genentech will be deemed to have terminated such Collaboration Program, effective as of the expiration date of the LSR Go Review Period, or the Dev Go Review Period, as applicable.

ARTICLE 3
TARGET NOMINATION AND SUBSTITUTION

3.1 Target Nomination.

3.1.1 Modulator Target Nomination. Genentech has the right to select, in its sole discretion, a total of up to four (4) Modulator Targets as Collaboration Targets under this Agreement, in each case, as set forth in the remainder of this Section 3.1.1.

(a) As of the Effective Date, Genentech has selected the two (2) Initial Collaboration Targets to be included as the subject of initial Discovery Research Activities under this Agreement.

(b) Subject to this ARTICLE 3, including Genentech's substitution and exchange rights hereunder, during the Expansion Option Period, Genentech has the right to select, in its sole discretion, a total of up to two (2) additional Modulator Targets as Collaboration Targets to be the subject of initial Discovery Research Activities under this Agreement, and potential Development and Commercialization of Discovery Constructs and Licensed Products incorporating such Discovery Constructs (each, an "**Expansion Option**"). Genentech may exercise each Expansion Option by (i) selecting such additional Modulator Targets from the list of Genentech Reserved Targets, or (ii) nominating any other Modulator Target pursuant to Section 3.1.3, provided that if such Nominated Target is an Unavailable Target, such Expansion Option shall not be deemed exercised.

(c) Notwithstanding Section 3.1.1(b), (i) if Genentech does not exercise an Expansion Option within [***], all Expansion Options will expire, and Genentech shall thereafter have no further right to nominate any additional Collaboration Targets to be the subject of Discovery Research Activities under this Agreement. For clarity, the total number of Genentech Reserved Targets prior to Genentech's exercise of any Expansion Option may not exceed two (2). Genentech shall be deemed to have timely exercised its Expansion Option(s) if

Genentech has delivered the Target Nomination Notice within the applicable time period specified in this Section 3.1.1(c), even if BicycleTx delivers the Target Availability Notice only after the expiry of such time period. For clarity, if Genentech has timely exercised an Expansion Option and BicycleTx indicates in the Target Availability Notice that the Modulator Target requested by Genentech in such Target Nomination Notice is an Unavailable Target, then Genentech may, within [***] after receipt of such Target Availability Notice, deliver a subsequent Target Nomination Notice for a different Modulator Target, even if such subsequent Target Nomination Notice is delivered after the expiry of the applicable time period set forth in this Section 3.1.1(c).

(d) Subject to [***] Section 3.1.1(c), if Genentech wishes to select a Genentech Reserved Target as a Collaboration Target, Genentech shall notify BicycleTx in writing, and upon payment of the Target Nomination Fee as set forth in Section 3.1.1(e), such Genentech Reserved Target shall automatically become a Collaboration Target hereunder.

(e) For each additional Modulator Target selected by Genentech pursuant to this Section 3.1.1, Genentech shall pay to BicycleTx a one-time payment (the "**Target Nomination Fee**") as set forth in Section 8.2.1.

3.1.2 Target Proposal. Prior to nomination of a Target (whether pursuant to Section 3.1.3 or Section 3.2), Genentech may, in its discretion, disclose a Target it is considering for potential nomination (a "**Proposed Target**") to BicycleTx and request in writing that BicycleTx confirm whether the Proposed Target is an Unavailable Target. BicycleTx shall notify Genentech in writing, within [***], whether such Nominated Target is an Unavailable Target. Notwithstanding anything herein to the contrary, (a) Genentech shall have no obligation to nominate any Proposed Targets, and (b) in no way shall a request by Genentech with respect to a Proposed Target under this Section 3.1.2 be deemed to be a nomination of the Target as a Collaboration Target (and such Target shall not be considered nominated unless and until it is formally nominated in accordance with the terms and conditions set forth in Section 3.1.3).

3.1.3 Target Nomination Process. To nominate a Modulator Target or Antigen Target other than a Genentech Reserved Target as a Collaboration Target, Genentech shall provide BicycleTx with a confidential written description of the applicable Modulator Target or Antigen Target (the "**Nominated Target**"), including, [***] such Modulator Target or Antigen Target (the "**Target Nomination Notice**"). Within [***] following BicycleTx's receipt of the Target Nomination Notice with respect to a Nominated Target, BicycleTx shall verify whether such Nominated Target is on its list of Unavailable Targets and notify Genentech in writing ("**Target Availability Notice**"). If the Target Availability Notice indicates that the Nominated Target is not on the list of Unavailable Targets, then, within [***] of such Target Availability Notice, the Parties will negotiate and mutually agree upon a Discovery Research Plan for such Nominated Target. Any such Discovery Research Plan shall be substantially similar in form and content to the Discovery Research Plan(s) for the previous Collaboration Target(s), including the Initial Discovery Research Plan, [***]. Thereafter, such Nominated Target shall be designated as a "**Collaboration Target**" on the date when (a) the Parties have agreed on such Discovery Research Plan, and (b) Genentech has paid the applicable Target Nomination Fee (the "**Target Acceptance Date**"), and the Parties will have all rights and obligations hereunder in connection with such Collaboration Target (including exclusivity in accordance with Section 7.8) as of the Target Acceptance Date.

3.1.4 Target Nomination Process for Adding a Target to the Genentech Reserved Target List. The nomination of an additional Target to the Genentech Reserved Target list shall follow the procedure set forth in Section 3.1.3 *mutatis mutandis*, except that (a) for clarity, such nomination of an additional Target to the Genentech Reserved Target list shall [***], (b) the Parties shall [***] at the time it is added to the Genentech Reserved Target list, and (c) at the time Genentech adds a Target to the Genentech Reserved Target list, it shall [***].

3.1.5 Gatekeeper. If either Party desires, at any time following the Effective Date, to make confidential inquiries regarding the availability of Modulator Targets or Antigen Targets (i.e. other than through the process set forth in Section 3.1.3), such Party shall notify the other Party in writing thereof. As soon as reasonably practicable following receipt of such notice, and in any case within [***] following receipt of such notice, BicycleTx shall engage an independent Third Party mutually agreeable to the Parties (the "**Gatekeeper**") for the purposes of performing the applicable functions set forth in Section 3.1.2 and Section 3.1.3, including (a) maintaining a list of Unavailable Targets and (b) issue the Target Availability Notice. The [***]. Such engagement shall be on terms consistent with this Agreement and mutually agreeable to the Parties, including provisions relating to confidentiality. The identity of the Unavailable Targets shall be deemed the Confidential Information of BicycleTx, and the identity of the Genentech Reserved Targets (if any), Proposed Targets, and Nominated Targets shall be deemed the Confidential Information of Genentech. Following the appointment of a Gatekeeper, (i) all references in Section 3.1.3 regarding disclosure by one Party to the other Party shall instead be deemed to refer to disclosure to or by the Gatekeeper by or to the applicable Party, *mutatis mutandis*, and (ii) BicycleTx shall notify the Gatekeeper of the Unavailable Targets promptly, but in no event later than [***]. Upon receipt of such notification, the Gatekeeper shall update the list of Unavailable Targets accordingly.

3.2 Target Substitution. Genentech shall have the right, from time to time during the Term, to substitute a different Modulator Target (or Targeting Arm, as applicable) in place of an existing Collaboration Target (each, a "**Target Substitution**") solely as set forth below:

3.2.1 [***] Substitution Right [***]. Subject to Section 3.2.7, [***] Genentech shall have the one-time right [***], to substitute during a period of [***] following the date of the receipt by Genentech [***] (the "**Initial Substitution Period**"), another available [***] Target, [***] (each, a "**Substitute Target**"), [***]. Such Substitute Target shall be nominated using *mutatis mutandis* the Target nomination process set forth in Section 3.1.3 or Section 3.1.4, as applicable. For clarity, [***] the nomination of the Substitute Target shall be effective as of Genentech's receipt of the Target Availability Notice.

3.2.2 [***] Substitution Right [***]. Subject to Section 3.2.6 and Section 3.2.7, [***], Genentech shall have the one-time-right [***] during a period following the [***] to nominate a Substitute Target, [***]. Such Substitute Target shall be nominated using *mutatis mutandis* the Target nomination process set forth in Section 3.1.3 or Section 3.1.4, as applicable. For clarity, [***] the nomination of the Substitute Target shall be effective as of Genentech's receipt of the Target Availability Notice.

3.2.3 [***] Substitution Right [***]. Subject to Section 3.2.7, [***] Genentech shall have the one-time right [***] during a period of [***] following the date [***], to nominate a Substitute Target [***]. Such Substitute Target shall be nominated using *mutatis mutandis* the Target nomination process set forth in Section 3.1.3 or Section 3.1.4, as applicable. For clarity, [***] the nomination of the Substitute Target shall be effective as of Genentech's receipt of the Target Availability Notice.

3.2.4 [***] Substitution Right [***]. Subject to Section 3.2.6 and Section 3.2.7, [***], Genentech shall have the one-time-right [***], during the period between [***], to nominate a Substitute Target. Such Substitute Target shall be nominated using *mutatis mutandis* the Target nomination process set forth in Section 3.1.3 or Section 3.1.4, as applicable, but [***].

3.2.5 [***] Substitution. [***], Genentech shall have a one-time right, [***], to nominate a Substitute Target [***]. Genentech may exercise such right at any time during [***]. Any substitution of a Target [***] will follow the Target nomination process set forth in Section 3.1.4. Following a substitution [***], the applicable Substitute Target [***].

3.2.6 Limitations on Substitution Right. Genentech may not (a) substitute a Target for any Modulator Target that was already designated as a Collaboration Target as a result of the operation of this Section 3.2, or (b) perform [***] Target Substitutions [***] Collaboration Program under [***].

3.2.7 Effects of Target Substitution. Following any Target Substitution as set forth in this Section 3.2, the applicable Substitute Target will become a Collaboration Target hereunder effective as of the newly established Target Acceptance Date for such Substitute Target and, effective as of such

newly established Target Acceptance Date, (a) the Parties will have all rights and obligations under this Agreement in connection with such Substitute Target as a Collaboration Target and (b) the replaced Modulator Target shall become a Terminated Target and shall no longer be a Collaboration Target. Following any Target Substitution, Genentech shall grant, and hereby does grant, effective upon the applicable Target Acceptance Date for the new Modulator Target, to BicycleTx and its Affiliates, as applicable, an Unblocking License for the applicable Terminated Target.

3.3 Genentech Reserved Targets. From the Effective Date until the earlier of (a) the expiration of the Expansion Option Period, or (b) the date upon which Genentech exercises its second Expansion Option, BicycleTx shall not, and shall cause its Affiliates not to, option, license, authorize, appoint, or otherwise enable any Third Party to, directly or indirectly, develop, commercialize or manufacture any Bicycle Construct, product, service, or therapy that is directed to any Genentech Reserved Target or otherwise enter into any arrangement or take any other action that would preclude a Genentech Reserved Target from being designated as a Collaboration Target hereunder. Upon the earlier of the dates set forth in subclause (a) or (b), the Genentech Reserved Target list will no longer apply.

ARTICLE 4
COLLABORATION MANAGEMENT

4.1 Joint Research Committee.

4.1.1 Formation. Within [***] after the Effective Date, the Parties shall establish a joint research committee (the "**JRC**"). The JRC shall consist of [***] representatives from each of the Parties (with the number of such representatives at each Party's election, but with each Party collectively having one (1) vote). Each representative shall have the requisite experience and seniority to enable such person to make decisions on behalf of the applicable Party with respect to the issues falling within the decision making authority of the JRC. From time to time, each Party may substitute one (1) or more of its representatives to the JRC on written notice to the other Party. Each Party shall select from its representatives a representative who will chair the JRC jointly with the selected representative from the other Party. Each Party may replace its co-chairperson from time to time by informing the other Party in writing.

4.1.2 Specific Responsibilities. The JRC shall develop the strategies for and oversee the Discovery Research Activities in accordance with the applicable Discovery Research Plan for each Collaboration Program, and shall serve as a forum for the coordination of such activities. In particular, the JRC shall:

(a) serve as a discussion forum in relation to potential Modulator Targets and Antigen Targets for inclusion as potential Collaboration Targets (including respective Substitute Targets, if any) during any period when the Parties have not elected to appoint a Gatekeeper;

(b) periodically (no less often than [***]) review and serve as a forum for discussing the Discovery Research Plan for each Collaboration Target, and review and approve any amendments thereto;

(c) oversee the conduct and progress of the Discovery Research Activities (including the need for potential amendments to the LSR Go and Dev Go Criteria), and discuss and agree upon any activities to be allocated for performance by Genentech (if any);

(d) monitor the achievement of (i) the Hit Success Criteria determining POP Achievement, (ii) the LSR Go Criteria, (iii) the Dev Go Criteria, and (iv) the Targeting Arm Criteria;

(e) monitor the completion of the activities and the generation of the data required to be included in the LSR Go Data Package and the Dev Go Data Package, as applicable in order to confirm whether all components of the LSR Go Data Package and the Dev Go Data Package, as applicable, are complete [***];

(f) prior to the commencement of the Lead Generation Phase for a Collaboration Program, discuss and agree upon the contents of the LSR Go Data Package [***];

(g) prior to the commencement of the Lead Validation Phase for a Collaboration Program, discuss and agree upon the contents of the Dev Go Data Package [***];

(h) discuss the scope of any modifications or improvements requested by Genentech to any Discovery Construct or Development Candidate pursuant to Section 5.2;

(i) serve as a forum for discussion of results from the conduct of the Discovery Research Activities;

(j) extend the Research Term as provided in Section 2.4.2;

(k) establish secure access methods (such as secure databases) for each Party to access research and discovery and other JRC related information and Know-How as contemplated under this Agreement;

(l) monitor and implement the transfer of CMC materials to Genentech, whether pursuant to Section 5.3 or Section 5.4;

(m) monitor and implement the technology transfer to Genentech pursuant to Section 5.4; and

(n) perform such other functions as are set forth herein or as the Parties may mutually agree in writing, except where in conflict with any provision of this Agreement.

4.2 General Provisions Applicable to the JRC.

4.2.1 Meetings and Minutes. The JRC shall meet [***], either in person or by tele-/videoconference with the venue of the in person meetings alternating between locations designated by BicycleTx and locations designated by Genentech. At least [***] the JRC representatives shall meet in person, unless otherwise agreed by the Parties. The Alliance Manager shall be permitted to attend any such JRC meetings. The chairperson of the JRC shall be responsible for calling meetings on no less than [***] notice. Each Party shall make all proposals for agenda items and shall provide all appropriate information with respect to such proposed items at least [***] in advance of the applicable meeting; provided

that under exigent circumstances requiring input by the JRC, a Party may provide its agenda items to the other Party within a shorter period of time in advance of the meeting, or may propose that there not be a specific agenda for a particular meeting, so long as the other Party consents to such later addition of such agenda items or the absence of a specific agenda for such meeting. The chairpersons of the JRC (or their designee) shall prepare and circulate minutes of each meeting within [***] after the meeting for the Parties' review and approval. The Parties shall agree on the minutes of each meeting promptly, but in no event later than within [***] following circulation of the draft minutes.

4.2.2 Procedural Rules. The JRC shall have the right to adopt such standing rules as shall be necessary for its work, so long as such rules are not inconsistent with this Agreement. A quorum of the JRC shall exist whenever there is present at a meeting at least one (1) representative appointed by each Party. Representation by proxy shall be allowed. The JRC shall take action by consensus of the representatives present at a meeting at which a quorum exists, with each Party having a single vote irrespective of the number of representatives of such Party in attendance, or by a written resolution signed by at least one (1) representative appointed by each Party. Employees or consultants of either Party that are not representatives of the Parties on the JRC may attend meetings of the JRC; provided that such attendees (a) shall not vote or otherwise participate in the decision-making process of the JRC, and (b) are bound by obligations of confidentiality and non-disclosure equivalent to those set forth in ARTICLE 11.

4.3 Decisions.

4.3.1 Decision Making Authority. The JRC shall decide matters within its responsibilities pursuant to Section 4.1.2.

4.3.2 Consensus; Good Faith. The members of the JRC shall in good faith cooperate with one another and shall endeavor to seek agreement with respect to issues to be decided by the JRC.

4.3.3 Final Decision Right; Dispute Resolution. If the JRC cannot, or does not, reach consensus on an issue, then (a) BicycleTx shall have final say on [***]; (b) [***] Genentech shall have final say on [***]; and (c) neither Party shall have final say on [***] that would [***]. In each of case Section 4.3.3(c)(i) and 4.3.3(c)(ii) above, the status quo shall persist unless and until the Parties' mutually agree. If the JRC does not reach consensus on [***], then the dispute shall first be referred to the Senior Officers of the Parties, who shall confer in good faith on the resolution of the issue. If the Senior Officers are unable to reach consensus on [***] for a given Collaboration Program, [***] provided: (1) any additional Discovery Research Activities resulting from such [***], (2) any additional Discovery Research Activities resulting from [***] shall not [***], (3) the [***] shall not [***]

[***] and (4) BicycleTx shall [***]. If BicycleTx [***], Genentech may [***] by Genentech. Notwithstanding the foregoing, neither Party shall use its final decision-making authority to (x) impose any requirement on the other Party to undertake obligations beyond those for which it is responsible or to forgo any of its rights under this Agreement, (y) require the other Party to violate any Applicable Law, ethical requirement, or any agreement it may have with any Third Party, or (z) amend the terms and conditions of this Agreement. Disputes arising between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith, and that are outside of the decision-making authority of the JRC, shall be finally resolved pursuant to Section 15.7.

4.4 Limitations on Authority. Each Party shall retain the rights, powers, and discretion granted to it under this Agreement and no such rights, powers, or discretion shall be delegated to or vested in the JRC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing. The JRC shall not have the power to amend, modify, or waive compliance with this Agreement, which may only be amended or modified as provided in Section 15.9 or compliance with which may only be waived as provided in Section 15.11.

4.5 Alliance Manager. Each Party shall appoint a person who shall oversee contact between the Parties for all matters between meetings of the JRC and shall have such other responsibilities as the Parties may agree in writing after the Effective Date (each, an "**Alliance Manager**"). Each Party may replace its Alliance Manager at any time by notice in writing to the other Party.

4.6 Discontinuation of the JRC. Following the date upon which [***] for a given Collaboration Program [***], the JRC shall have no further responsibilities or authority under this Agreement with respect to that Collaboration Target and the associated Compounds and Licensed Products. Once the applicable [***], the JRC will be considered fully dissolved by the Parties. Notwithstanding the above, if BicycleTx agrees to conduct Additional Discovery Activities pursuant to Section 5.2, the JRC shall be reinstated to oversee such Additional Discovery Activities until the completion thereof.

4.7 Interactions Between a Committee and Internal Teams. The Parties recognize that each Party possesses an internal structure (including various committees, teams and review boards) that will be involved in administering such Party's activities under this Agreement. Nothing contained in this Article shall prevent a Party from making routine day-to-day decisions relating to the conduct of those activities for which it has a performance or other obligation hereunder, in each case in a manner consistent with the then-current applicable Discovery Research Plan and the terms and conditions of this Agreement.

4.8 Working Groups. From time to time, the JRC may establish and delegate duties to sub-committees or directed teams (each, a "**Working Group**") on an "as-needed" basis to oversee particular projects or activities (for example, joint project team, joint finance group, and/or joint intellectual property group). Each such Working Group shall be constituted and shall operate as the JRC determines; provided that each Working Group shall have equal representation from each Party, unless otherwise mutually agreed. Working Groups may be established on an ad hoc basis for purposes of a specific project or on such other basis as the JRC may determine. Each Working Group and its activities shall be subject to the oversight, review and approval of, and shall report to, the JRC. In no event shall the authority of the

Working Group exceed that specified for the JRC. All decisions of a Working Group shall be by consensus. Any disagreement between the designees of Genentech and BicycleTx on a Working Group shall be referred to the JRC for resolution.

4.9 Expenses. Each Party shall be responsible for all travel and related costs and expenses for its members and other representatives to attend meetings of, and otherwise participate on, the JRC or any Working Group.

ARTICLE 5
DEVELOPMENT AND REGULATORY

5.1 Development of Licensed Products following Dev Go. For each Collaboration Program, following Genentech's delivery of the Dev Go Notice, except for any activities that BicycleTx agrees to conduct in accordance with Section 5.2, Genentech shall have the sole right to Develop and Manufacture, including seeking Regulatory Approvals for, Compounds and Licensed Products directed to the applicable Collaboration Target(s) in the Field and in the Territory, in each case at Genentech's sole expense. On a Collaboration Program-by-Collaboration Program basis, following the date of the Dev Go Notice for such Collaboration Program and delivery to Genentech of the applicable Compound(s) and the completion of the technology transfer pursuant to Section 5.4.1, Genentech shall use Commercially Reasonable Efforts to Develop and obtain Regulatory Approval for a Licensed Product comprising or containing a Development Candidate arising from such Collaboration Program in at least one Indication for use in each Major Market. Genentech shall have the right to satisfy its diligence obligations under this Section 5.1 through its Affiliates or Sublicensees. For each Collaboration Target, following the date of [***], Genentech will provide to BicycleTx [***] reports within [***] summarizing the key Development activities undertaken and summarizing the results achieved with respect to the applicable Discovery Constructs and Licensed Products [***]. Following the delivery of each report, Genentech will make appropriate personnel available to BicycleTx during business hours and on reasonable advanced notice to answer reasonable questions regarding the information contained in such report, [***].

5.2 Additional Discovery Activities After Dev Go Notice. On a Collaboration Program-by-Collaboration Program basis, at any time following Genentech's delivery of a Dev Go Notice for the then-current Development Candidate for such Collaboration Program, Genentech may request that BicycleTx provide certain reasonable research and development assistance (a) to [***] and/or (b) [***] (all such activities in (a) and (b), the "**Additional Discovery Activities**"). If Genentech makes such a reasonable request, BicycleTx shall consider such request and, [***] such Additional Discovery Activities, provided that Genentech shall compensate BicycleTx for BicycleTx's [***] costs ([***]) incurred in the performance of such Additional Discovery Activities. For clarity, [***]

[***] such Additional Discovery Activities. If, as a result of any such Additional Discovery Activities Genentech selects an alternative Compound to advance into further pre-clinical Development, such alternative Compound will thereafter be deemed the Development Candidate for the applicable Collaboration Target. Notwithstanding the foregoing, if BicycleTx does not agree to conduct any such Additional Discovery Activities ([***]), Genentech may conduct such Additional Discovery Activities (or have a Third Party conduct such Additional Discovery Activities) and if, as a result of Genentech's or its designated Third Party's performance of such Additional Discovery Activities, Genentech selects an alternative Compound to further modify and advance into further pre-clinical Development, such alternative compound shall be deemed a "**Modified Compound**", provided that Genentech (itself or through its Affiliate or Third Party) shall not be permitted to select any Modified Compound to advance into further Development activities unless such Modified Compound (i) [***] and (ii) is directed to and binds the same Collaboration Target as the applicable Compound. For clarity, (x) [***] under this Agreement, [***], in each case [***] and, (y) [***] under this Agreement [***].

5.3 Transfer of CMC Materials [***]. On a Collaboration Program-by-Collaboration Program basis, Genentech may request [***], that BicycleTx conduct a manufacturing technology transfer to enable Genentech to conduct certain CMC Activities in connection with Compounds and Licensed Products arising from such Collaboration Program [***]. Genentech's request shall include a summary of the CMC Activities that Genentech intends to conduct (which shall be reasonable for the stage of development of the applicable Collaboration Program), and the Parties shall, prior to any transfer, agree upon a plan for the transfer of CMC materials necessary for such specified CMC Activities. For clarity, [***]. BicycleTx shall initiate such transfer within [***] following the receipt of such request (and following agreement on the plan for such CMC Activities), which shall include a transfer of [***] to enable Genentech or Genentech's designees to conduct the CMC Activities to be conducted by Genentech. BicycleTx shall [***] such transfer of CMC materials, provided that (i) if Genentech [***], then Genentech shall [***], and (ii) if Genentech [***], Genentech shall [***]. For clarity, Genentech shall [***] at Genentech's request for CMC Activities [***]

[***]. Furthermore, if Genentech [***], BicycleTx may elect to buy any Compound and/or materials resulting from such CMC Activities ([***]) at Genentech's [***] cost to manufacture. Inventory and any CMC materials that BicycleTx or BicycleTx's designees are to provide to Genentech shall be shipped [***].

5.4 Technology Transfer [***]. On a Collaboration Target-by-Collaboration Target basis following Genentech's delivery of the Dev Go Notice for the applicable Collaboration Program:

5.4.1 As soon as reasonably practicable following Genentech's delivery of the applicable Dev Go Notice (and in any event not more than [***]), BicycleTx shall, and shall cause its Affiliates to, without additional compensation, disclose and make available to Genentech (which obligation may include granting personnel designated by Genentech controlled access to an electronic data room), in such form as maintained by BicycleTx in the ordinary course of business, BicycleTx Know-How and Joint Know-How (to the extent such Joint Know-How is in BicycleTx's possession), and a list of the BicycleTx Patents and Joint Collaboration Patents, in each case to the extent [***] for the Exploitation of the Compounds for such Collaboration Program. For clarity, the BicycleTx Know-How provided pursuant to this Section 5.4.1 shall include BicycleTx Know-How [***] to perform CMC Activities in respect of the relevant Development Candidate [***].

5.4.2 BicycleTx shall provide Genentech [***] in order to transfer to Genentech the BicycleTx Know-How and Joint Collaboration Know-How required to be produced pursuant to Section 5.4.1. Without prejudice to the generality of the foregoing, if [***] are reasonably requested by Genentech [***], BicycleTx shall [***] mutually agreed by the Parties. BicycleTx shall provide up to [***] to Genentech pursuant to this Section 5.4.2. For any [***] requested by Genentech and provided by BicycleTx in excess of [***], Genentech shall reimburse BicycleTx [***].

5.5 Subcontracting. Each Party shall have the right to subcontract any of its Development activities to a Third Party (a "**Third Party Provider**"); provided that solely with respect to Third Party Providers performing services that are [***], BicycleTx shall [***] to such Third Party Provider and the activities to be subcontracted. Genentech shall [***] set forth in this Section5.5 above; provided that [***]. BicycleTX shall obtain a written undertaking from each Third Party Provider that it will comply with the applicable terms and conditions of this Agreement, including the confidentiality provisions of ARTICLE 11.

5.6 Regulatory Matters.

5.6.1 Regulatory Activities.

(a) As between the Parties, Genentech, at its sole expense, shall have the sole right to prepare, obtain, and maintain the Drug Approval Applications (including the setting of the overall regulatory strategy therefor), other Regulatory Approvals and other regulatory submissions, including INDs, and to conduct communications with the Regulatory Authorities, for Compounds or Licensed Products in the Territory. Upon Genentech's request [***], BicycleTx shall provide Genentech with reasonable assistance in obtaining Regulatory Approvals for the Licensed Products, including providing necessary documents or other materials required by Applicable Law to obtain such Regulatory Approvals, provided that [***], and provided further that nothing in this Section 5.6.1 shall obligate BicycleTx to generate any additional data or other Know-How.

(b) All Regulatory Documentation (including all Regulatory Approvals and Product Labeling) specifically relating to Compounds or Licensed Products with respect to the Territory shall be owned by, and shall be the sole property and held in the name of, Genentech or its designated Affiliate, Sublicensee or designee. BicycleTx shall duly execute and deliver, or cause to be duly executed and delivered, such instruments and shall do and cause to be done such acts and things, including the filing of such assignments, documents, and instruments, as may be necessary under, or as Genentech may reasonably request in connection with this Section 5.6.

5.6.2 Recalls. Genentech shall notify BicycleTx promptly following its determination that any event, incident, or circumstance has occurred that may result in the need for a recall, market suspension, or market withdrawal of a Licensed Product in the Territory, and shall include in such notice the reasoning behind such determination and any supporting facts. Genentech (or its Sublicensee) shall have the right to make the final determination whether to voluntarily implement any such recall, market suspension, or market withdrawal in the Territory. If a recall, market suspension, or market withdrawal is mandated by a Regulatory Authority in the Territory, Genentech (or its Sublicensee) shall initiate such a recall, market suspension, or market withdrawal in compliance with Applicable Law. For all recalls, market suspensions or market withdrawals undertaken pursuant to this Section 5.6.2, Genentech (or its Sublicensee) shall be solely responsible for the execution thereof, and BicycleTx shall reasonably cooperate in all such recall efforts, at Genentech's request and expense.

5.6.3 Records. Each of BicycleTx and Genentech shall, and shall ensure that its Third Party Providers, maintain records in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, and in compliance with Applicable Law, which shall be complete and accurate and shall properly reflect all work done and results achieved in the performance of its Discovery Research Activities and Development activities hereunder, which shall record only such activities and shall not include or be commingled with records of activities outside the scope of this Agreement. Such records shall be retained by BicycleTx or Genentech, as the case may be, for at least [***] after the termination of this Agreement, or for such longer period as may be required by Applicable Law.

ARTICLE 6
COMMERCIALIZATION

6.1 In General. Genentech (itself or through its Affiliates or Sublicensees) shall have the sole right to Commercialize Compounds and Licensed Products in the Territory at its own cost and expense.

6.2 Commercialization Diligence. For each Collaboration Target, Genentech shall use Commercially Reasonable Efforts to Commercialize one Licensed Product in each Major Market following receipt of Regulatory Approval therefor in such Major Market, provided that (a) the Commercialization of Licensed Product [***], and (b) Genentech shall have the right to satisfy its diligence obligations under this Section 6.2 through its Affiliates and Sublicensees. With respect to a particular Collaboration Target, if Genentech [***] Compound or Licensed Product directed to such Collaboration Target, [***] Compound or Licensed Product directed to such Collaboration Target.

6.3 Product Trademarks. Genentech shall have the sole right to determine and own the Product Trademarks to be used with respect to the Exploitation of the Licensed Products on a worldwide basis. [***] with respect thereto or use [***] the Product Trademarks. Notwithstanding the foregoing, to the extent required by Applicable Law in a country or other jurisdiction in the Territory, the promotional materials, packaging, and Product Labeling for the Licensed Products used by Genentech and its Affiliates in connection with the Licensed Products in such country or other jurisdiction shall contain (a) the corporate name of BicycleTx (and to the extent required, BicycleTx grants Genentech a license, with the right to sublicense, to use the same for such purpose), and (b) the logo and corporate name of the manufacturer (if other than Genentech or an Affiliate).

6.4 Commercial Supply of Compounds or Licensed Products. As between the Parties, Genentech shall have the sole right, at its expense, to Manufacture (or have Manufactured) and supply Compounds and Licensed Products for commercial sale in the Territory by Genentech and its Affiliates and Sublicensees.

ARTICLE 7
GRANT OF RIGHTS

7.1 Grants to Genentech.

7.1.1 Effective upon Genentech's delivery to BicycleTx of a Dev Go Notice pursuant to Section 2.5.2(d), on a Collaboration Program-by-Collaboration Program basis, BicycleTx (on behalf of itself and its Affiliates) hereby grants to Genentech an exclusive (including with regard to BicycleTx and its Affiliates, except as provided in Section 7.6) license, with the right to grant sublicenses in accordance with Section 7.4, under (a) the BicycleTx Patents and BicycleTx Know-How, and (b) BicycleTx's interest in the Joint Collaboration Patents and in the Joint Collaboration Know-How (collectively, the "**BicycleTx**

IP") that is reasonably necessary or useful to Exploit the Compounds and corresponding Licensed Products in the Field in the Territory.

7.1.2 Effective upon the Effective Date or, as the case may be, upon the applicable Target Acceptance Date and during the Research Term under this Agreement, BicycleTx hereby grants to Genentech, on a Collaboration Target-by-Collaboration Target basis, a limited, non-exclusive, royalty-free license, without the right to grant sublicenses (but, for clarity, with the right to subcontract), under the BicycleTx IP solely to enable Genentech to perform Discovery Research Activities to be conducted by Genentech pursuant to Section 2.4.1 (if any) and to perform CMC Activities to be conducted by Genentech pursuant to Section 5.3 (if any).

7.2 Grants to Bicycle. Effective upon the Effective Date and during the Research Term (and thereafter for the performance of Additional Discovery Activities pursuant to Section 5.2.), Genentech hereby grants to BicycleTx, on a Collaboration Target-by-Collaboration Target basis, a non-exclusive, royalty-free license, without the right to grant sublicenses (other than to permitted subcontractors of BicycleTx in accordance with Section 5.5), under the Genentech Patents, Genentech Know-How, and Genentech's interests in the Joint Collaboration Patents and the Joint Collaboration Know-How solely for purposes of performing BicycleTx's obligations under, and as set forth in, the Discovery Research Plan(s).

7.3 Mutual Grants. Each Party hereby grants to the other Party a perpetual, irrevocable, non-exclusive, royalty-free, and fully paid-up license for all internal research purposes, without the right to grant sublicenses, under [***] a Collaboration Program hereunder, excluding [***] (a) in connection with [***], (b) solely with respect to [***], provided that [***], or (c) solely with respect to [***] as part of the [***], provided that [***]. It is understood and agreed that no commercial license is granted by either Party under this Section 7.3 (including but not limited to any license or other right to sell, offer for sale or otherwise commercialize any Compounds). It is further understood that the Parties shall have the right to [***] activities. Notwithstanding anything to the contrary herein, the Parties [***] the use of [***], and as such each Party agrees that the [***]; provided that: (a) [***] such use; (b) the foregoing [***], and will not be [***](i) a right to [***], or (ii) a [***]; and (c) [***] outside this Agreement.

7.4 Sublicenses. Genentech shall have the right to grant sublicenses, through multiple tiers of sublicensees, under the licenses granted in Section 7.1 to its Affiliates and Third Parties; provided that (a) each such sublicense shall be consistent with the terms and conditions of this Agreement, including terms of confidentiality and non-use no less restrictive than those set forth in this Agreement, (b) Genentech may not grant to any Third Party any rights to prosecute or enforce any BicycleTx Background Patents or BicycleTx Collaboration Patents, and (c) Genentech shall remain directly liable to BicycleTx with respect to its obligations under this Agreement and for the performance and acts and omissions of all sublicensees. As soon as reasonably practicable (but in any case within [***]) after the execution of any such sublicense agreement, Genentech shall provide BicycleTx with written notice thereof, including the identity of the Sublicensee and the scope of the license granted.

7.5 Distributorships. Genentech shall have the right, in its sole discretion, to appoint its Affiliates, and Genentech and its Affiliates shall have the right, in their sole discretion, to appoint any Third Party, in the Territory or in any country or other jurisdiction of the Territory, to distribute, market, and sell the Licensed Products. If Genentech or its Affiliates appoints such a Third Party that does not have rights to, and does not, Manufacture any Licensed Product (except solely to package or label such Licensed Product purchased in bulk form from Genentech or its Affiliates), such Third Party shall be a "**Distributor**" for purposes of this Agreement.

7.6 Retention of Rights. Notwithstanding the exclusive licenses granted to Genentech pursuant to Section 7.1.1 during the Term, BicycleTx shall retain all rights under the BicycleTx Background Patents, the BicycleTx Collaboration Patents, the BicycleTx Background Know-How, the BicycleTx Collaboration Know-How, BicycleTx's interests in the Joint Collaboration Patents and in the Joint Know-How, Regulatory Approvals and any other Regulatory Documentation (i) to perform, and to subcontract pursuant to Section 5.5 its obligations under this Agreement, (ii) to Exploit any and all Existing Targeting Arms and BicycleTx Future Independent Targeting Arms, in connection with any Target (including any Modulator Target or Antigen Target) other than a Collaboration Target, (iii) for any purpose outside the scope of the licenses and rights granted under Section 7.1, including to develop, manufacture and commercialize any products or services other than Compounds and Licensed Products, subject to Section 7.8. For clarity, nothing in this Section 7.6 shall imply that BicycleTx may retain any right with regard to Genentech Reserved Targets prior to the expiry of the Expansion Options as set forth in Section 3.1.1(c).

7.7 No Implied Licenses. Except as expressly provided herein, BicycleTx grants no other right or license to Genentech hereunder, including any rights or licenses to the BicycleTx Background Patents, the BicycleTx Program Patents, the BicycleTx Background Know-How, the BicycleTx Program Know-How, BicycleTx's interests in the Joint Collaboration Patents and the Joint Collaboration Know-How, or any other Patent or intellectual property rights not otherwise expressly granted herein. Except as expressly provided herein, Genentech grants no other right or license to BicycleTx hereunder, including any rights or licenses to the Genentech Background Patents, the Genentech Collaboration Patents, the Genentech Background Know-How, the Genentech Collaboration Know-How, or any other Patent or intellectual property rights not otherwise expressly granted herein.

7.8 Exclusivity.

7.8.1 With respect to each Modulator Target, during the applicable Target Exclusivity Period, neither BicycleTx nor any of its Affiliates shall (a) on BicycleTx's behalf or on behalf of (or in collaboration with) a Third Party, use BicycleTx IP or otherwise conduct activities to discover, design or identify compounds that bind to or modulate such Modulator Target, or (b) either directly or indirectly,

appoint or otherwise authorize or facilitate any Third Party to perform any of the activities set forth in the foregoing clause (a) (collectively, the "**Exclusivity Obligations**"). Notwithstanding the foregoing, the conduct by BicycleTx or its Affiliates of any of the foregoing activities with respect to any compound that binds to or modulates a Modulator Target, where (i) [***], and (ii) [***], shall not be deemed to be a breach of the Exclusivity Obligations.

7.8.2 For each Modulator Target, the Exclusivity Obligations shall commence (a) on the Effective Date for the Initial Collaboration Targets and initial Genentech Reserved Targets, (b) on the date a new Genentech Reserved Target is added to the list for Genentech Reserved Targets pursuant to Section 3.1.4, (c) on the Target Acceptance Date for a Target deemed a Collaboration Target as a result of Genentech's exercise of an Expansion Option pursuant to Section 3.1.1(b), and (d) on the applicable Target Acceptance Date for a Substitute Target. The Exclusivity Obligations shall continue (x) for each Collaboration Target, until the earlier of (i) [***] Collaboration Target or (ii) the termination of this Agreement with respect to the applicable Collaboration Program pursuant to Section 2.5.3 or Section 14.2, (y) for Genentech Reserved Targets, until the expiration of the Expansion Options as set forth in Section 3.1.1(c), and (z) for all Targets under this Agreement, until the termination of this Agreement in its entirety. The period in which the Exclusivity Obligations are in effect is referred to as the "**Target Exclusivity Period**".

ARTICLE 8
PAYMENTS AND RECORDS

8.1 Upfront Payment. Within fifteen (15) Business Days after the Effective Date, Genentech shall pay BicycleTx an one-time, non-refundable, non-creditable payment in the amount of Thirty Million Dollars ($30,000,000).

8.2 Target Nomination; Targeting Arms.

8.2.1 Promptly following the exercise of an Expansion Option by Genentech pursuant to Section 3.1.1 and after the Parties' agreement on the applicable Discovery Research Plan for such Nominated Target, BicycleTx shall issue an invoice for payment of a Target Nomination Fee of Ten Million Dollars ($10,000,000), and Genentech shall pay to BicycleTx such Target Nomination Fee within [***] following receipt of such invoice. For clarity, the maximum aggregate amount payable by Genentech under this Section 8.2.1 is Twenty Million Dollars ($20,000,000) (i.e., if Genentech exercises both Expansion Options under Section 3.1.1(b) and as a result two (2) Nominated Targets become Collaboration Targets).

8.2.2 Simultaneous with or promptly following BicycleTx's delivery of the Target Availability Notice for a Genentech Antigen Target, BicycleTx shall issue an invoice for payment of [***] for activities to be performed by BicycleTx on a Targeting Arm directed to such Genentech Antigen Target, and Genentech shall pay to BicycleTx such amount within [***] following receipt of such invoice.

8.2.3 Promptly following the Targeting Arm Data Package Acceptance Date for a given Targeting Arm, BicycleTx shall issue an invoice for payment by Genentech of [***], and Genentech shall pay to BicycleTx such amount within [***] following receipt of such invoice.

8.3 Target Substitution. Promptly following the receipt by Genentech of the Target Availability Notice for a [***], BicycleTx shall issue an invoice to Genentech for an [***], and Genentech shall pay to BicycleTx such [***] following receipt of such invoice.

8.4 Discovery Milestones. In partial consideration of the rights granted by BicycleTx to Genentech hereunder and subject to the terms and conditions set forth in this Agreement, Genentech shall pay to BicycleTx a non-refundable milestone payment after the achievement of each of the following milestones for the first Compound or Licensed Product, as applicable, for each Collaboration Target (irrespective of whether such Collaboration Target is an initially nominated Collaboration Target or a Substitute Target). Upon the achievement of each of the following milestone events, BicycleTx shall promptly issue an invoice for the applicable milestone payment and Genentech shall pay such milestone payment within [***] after receipt of such invoice from BicycleTx. Such milestone payments shall be as follows:

8.4.1 upon the delivery of the LSR Go Notice for each Modulator Target, [***];

8.4.2 upon the delivery of the Dev Go Notice for each Initial Collaboration Target, [***]; and

8.4.3 upon the delivery of the Dev Go Notice for each Modulator Target other than the Initial Collaboration Targets, [***].

8.5 Development, Regulatory and First Commercial Sale Milestones.

8.5.1 Development, Regulatory and First Commercial Sale Milestone Payments. In partial consideration of the rights granted by BicycleTx to Genentech hereunder and subject to the terms and conditions set forth in this Agreement, on a Modulator Target-by-Modulator Target basis, Genentech shall pay to BicycleTx a non-refundable milestone payment after the achievement of each of the following milestones for the first Licensed Product directed to a given Modulator Target, calculated as follows:

Development Milestone [***]	Milestone Payment Amount
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**

[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**

8.5.2 If the first Licensed Product directed to a given Modulator Target also incorporates [***] Targeting Arm, then for the first such Licensed Product incorporating such [***] Targeting Arm, the milestone payment for the Development Milestone #2 in the table above [***] shall be [***] instead of [***].

8.5.3 Development Milestones [***] set forth in the table above shall only be payable once for a given Modulator Target. Notwithstanding Section 8.5.1, Development Milestones #3-13 set forth in the table above shall each be payable for [***] Licensed Product targeting the same Modulator Target. If the Licensed Product contains a [***] of a [***], then the amount of each milestone payment above shall be [***] for such Modified Compound.

8.5.4 On a Modulator Target-by-Modulator Target basis, if a development milestone payment set forth in this Section 8.5 for a Licensed Product becomes due before an earlier listed development milestone payment for such Licensed Product, then the earlier listed development milestone payment shall become payable upon the achievement of the later listed development milestone.

8.5.5 Genentech shall notify BicycleTx within [***] after achieving any milestone set forth in the table above. Following such notice BicycleTx shall promptly issue an invoice for the corresponding milestone payment and Genentech shall pay the development milestone payment within [***] after receipt of such invoice from BicycleTx.

8.6 Sales-Based Milestones. In partial consideration of the rights granted by BicycleTx to Genentech hereunder and subject to the terms and conditions set forth in this Agreement, on a Licensed Product-by-Licensed Product basis, Genentech shall pay to BicycleTx the following non-refundable milestone payments due within [***] after the end of the Calendar Quarter in which such milestone was achieved with respect to Net Sales of each Licensed Product calculated as follows: [***].

Each milestone payment in this Section 8.6 shall be payable only upon the first achievement of such milestone for a given Licensed Product. The maximum aggregate amount payable by Genentech pursuant to this Section 8.6 for each Licensed Product is Two Hundred Million Dollars ($200,000,000).

8.7 Royalties.

8.7.1 Royalty Rates. As further consideration for the rights granted to Genentech hereunder, subject to Section 8.7.3, commencing upon the First Commercial Sale of a Licensed Product in the Territory, on a Licensed Product-by-Licensed Product basis, Genentech shall pay to BicycleTx a non-refundable royalty on Net Sales of each Licensed Product in the Territory (excluding Net Sales of each Licensed Product in any country or other jurisdiction in the Territory for which the Royalty Term for such

Licensed Product in such country or other jurisdiction has expired) during each Calendar Year at the following rates:

Calendar Year Net Sales in the Territory of a given Licensed Product in a Calendar Year	Royalty Rate
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
[***]	**[***]**

8.7.2 Royalty Term. Genentech shall have no obligation to pay any royalty with respect to Net Sales of any Licensed Product in any country or other jurisdiction after the Royalty Term for such Licensed Product in such country or other jurisdiction has expired.

8.7.3 Reductions. Notwithstanding the foregoing:

(a) If following the first market entry of a Generic Product of a Licensed Product in a given country in the Territory during the Royalty Term for such Licensed Product in such country, there has been in any Calendar Quarter after such entry a decline of the Sales of such Licensed Product in such country greater than [***] of the average level of the Sales of such Licensed Product achieved in such country [***] immediately preceding such Calendar Quarter (such percentage drop in Sales following the first market entry of a Generic Product, a "**Generic Entry**"), then, except as set forth in Section 8.7.3(c) below, the applicable royalty rate on the Net Sales of such Licensed Product in such country shall be reduced to [***] for the remainder of the applicable Royalty Term for such Licensed Product in such country.

(b) Genentech shall be entitled to deduct from any royalties payable hereunder with respect to a Licensed Product for a particular country or other jurisdiction [***] of all [***] paid under Genentech In-License Agreements with respect to such Licensed Product for such country or other jurisdiction; provided that in no case shall such deduction effectively reduce such royalties set forth in Section 8.7.1 below the royalties that would be payable under the royalty rates set forth in Section 8.7.3(d). [***]

[***], subject to the preceding proviso.

(c) If in a given country in the Territory in a Calendar Quarter during the Royalty Term for a Licensed Product such Licensed Product is not Covered by a Valid Claim of a [***] that Covers [***] such Licensed Product in such country, the royalty rate set forth in Section 8.7.1 with respect to such Licensed Product in such country shall be replaced by the royalty rates set forth in Section 8.7.3(d) for such Calendar Quarter; provided that following the tenth (10^{th}) anniversary of the First Commercial Sale of a Licensed Product in a country, if the last Valid Claim of a [***] that Covers such Licensed Product in such country only Covers [***] such Licensed Product, then [***].

(d) Except as set forth in Section 8.7.3(a), the cumulative reductions set forth in this Section 8.7.3 shall not reduce the royalties payable to BicycleTx on any Licensed Product in any Calendar Quarter to less than the amounts set forth in the table below at each royalty tier.

Calendar Year Net Sales in the Territory of a given Licensed Product in a Calendar Year	**Royalty Floor**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

8.8 Royalty Payments and Reports. Genentech shall calculate all amounts payable to BicycleTx pursuant to Section 8.7 at the end of each Calendar Quarter, which amounts shall be converted to Dollars, in accordance with Section 8.9. Genentech shall pay to BicycleTx the royalty amounts due with respect to a given Calendar Quarter within [***] after the end of such Calendar Quarter. Each payment of royalties due to BicycleTx shall be accompanied by a statement of the amount of Net Sales of each Licensed Product in each country or other jurisdiction the Territory during the applicable Calendar Quarter (including such amounts expressed in local currency and as converted to Dollars) and a calculation of the amount of royalty payment due on such Net Sales for such Calendar Quarter and whether any sales milestone under Section 8.6 has been achieved.

8.9 Mode of Payment. All payments to either Party under this Agreement shall be made by deposit of Dollars in the requisite amount to such bank account as the receiving Party may from time to time designate by written notice to the paying Party. For the purpose of calculating any sums due under, or otherwise reimbursable pursuant to, this Agreement (including the calculation of Net Sales expressed in currencies other than Dollars), a Party shall convert any amount expressed in a foreign currency into Dollar equivalents using its, its Affiliate's or Sublicensee's standard conversion methodology consistent with Accounting Standards.

8.10 [***]. For clarity, [***].

8.11 Withholding Taxes.

8.11.1 Withholding Amounts. If any sum due to be paid to either Party hereunder is subject to any withholding or similar tax, the Parties shall use their commercially reasonable efforts to do all such acts and to sign all such documents as will enable them to take advantage of any applicable double taxation agreement or treaty. In the event there is no applicable double taxation agreement or treaty, or if an applicable double taxation agreement or treaty reduces but does not eliminate such withholding or similar tax, the payor shall remit such withholding or similar tax to the appropriate government authority, deduct the amount paid from the amount due to payee and secure and send to payee the best available evidence of the payment of such withholding or similar tax. Except as otherwise provided in this Agreement, any such amounts deducted by the payor in respect of such withholding or similar tax shall be treated as having been paid by the payor for purposes of this Agreement. If withholding or similar taxes are paid to a government authority, each Party will provide the other such assistance as is reasonably required to obtain a refund of the withheld or similar taxes, or to obtain a credit with respect to such taxes paid.

8.11.2 Withholding Actions. Notwithstanding the foregoing, the Parties acknowledge and agree that if Genentech (or its assignee pursuant to Section 15.3) is required by Applicable Law to withhold taxes in respect of any amount payable under this Agreement, and if such withholding obligation arises as a result an assignment of this Agreement as permitted under Section 15.3, [***], then notwithstanding anything to the contrary herein, any such [***]. BicycleTx shall [***]. Notwithstanding the foregoing, the Parties acknowledge and agree that as of the date of this Agreement and under Applicable Laws, no withholding tax will be applicable to payments made to BicycleTx pursuant to this Agreement [***].

8.12 Taxes. BicycleTx shall pay all sales, turnover, income, revenue, value added, and other taxes levied on account of any payments accruing or made to BicycleTx under this Agreement. If provision is made in law or regulation of any country for withholding of taxes of any type, levies or other charges with respect to any royalty or other amounts payable under this Agreement to BicycleTx, then Genentech shall promptly pay such tax, levy or charge for and on behalf of BicycleTx to the proper governmental authority, and shall promptly furnish BicycleTx with receipt of payment. Genentech shall be entitled to deduct any such tax, levy or charge actually paid from royalty or other payment due to BicycleTx or be promptly reimbursed by BicycleTx if no further payments are due to BicycleTx. Each Party agrees to reasonably assist the other Party in claiming exemption from such deductions or withholdings under double taxation or similar agreement or treaty from time to time in force and in minimizing the amount required to be so withheld or deducted.

8.13 Interest on Late Payments. If any payment due to either Party under this Agreement is not paid when due, then such paying Party shall pay interest thereon (before and after any judgment, but excluding the period during which termination is tolled pursuant to Section 14.3.1) at [***], such interest to run from the date on which payment of such sum became due until payment thereof in full together with such interest.

8.14 Audit. Genentech shall, shall cause its Affiliates to, and shall use commercially reasonable efforts to cause its Sublicensees to keep complete and accurate books and records pertaining to Net Sales of Licensed Products in sufficient detail to calculate all amounts payable hereunder. At the request and expense of BicycleTx, Genentech shall permit an independent public accounting firm of nationally recognized standing designated by BicycleTx and reasonably acceptable to Genentech, at reasonable times during normal business hours and upon [***] prior written notice, to audit the books and records maintained pursuant to this Section 8.14 to ensure the accuracy of all reports and payments made hereunder. Such examinations may not (a) be conducted for any Calendar Year more than [***] after the end of such Calendar Year, (b) be conducted more than once in any [***] period or (c) be repeated for any Calendar Year. The accounting firm shall disclose to BicycleTx only whether the reports are correct or not, and the specific details concerning any discrepancies. No other information shall be shared with BicycleTx. Except as provided below, the cost of an audit pursuant to this Section 8.14 shall be borne by BicycleTx, unless the audit reveals an underpayment owed by Genentech of more than [***] from the reported amounts, in which case Genentech shall bear the cost of such audit.

8.15 Audit Dispute. In the event of any good faith dispute with respect to any audit under Section 8.14, BicycleTx and Genentech shall work in good faith to promptly resolve the disagreement. If the Parties are unable to reach a mutually acceptable resolution of any such dispute within [***], the dispute shall be submitted for resolution to a certified public accounting firm jointly selected by each Party's certified public accountants or to such other Person as the Parties shall mutually agree (the "**Audit Expert**"). The decision of the Audit Expert shall be final and the costs of such decision-making as well as the initial audit shall be borne between the Parties in such manner as the Audit Expert shall determine. Not later than [***] after such decision and in accordance with such decision, Genentech shall pay any underpaid amounts or BicycleTx shall reimburse any overpaid payments, as applicable.

8.16 Confidentiality. The receiving Party shall use all information subject to review under this ARTICLE 8 only for the purpose of verifying royalty statements and payment amounts and treat all such information as Confidential Information in accordance with the confidentiality provisions of ARTICLE 11 and the Parties shall cause the Audit Expert and the independent public accounting firm of nationally

recognized standing designated by BicycleTx pursuant to Section 8.14 to enter into a reasonably acceptable confidentiality agreement with Genentech obligating such firm to retain all such financial information in confidence pursuant to such confidentiality agreement.

8.17 No Other Compensation. Each Party hereby agrees that the terms of this Agreement fully define all consideration, compensation and benefits, monetary or otherwise, to be paid, granted or delivered by one (1) Party to the other Party in connection with the transactions contemplated herein. Neither Party previously has paid or entered into any other commitment to pay, whether orally or in writing, any of the other Party's employees, directly or indirectly, any consideration, compensation or benefits, monetary or otherwise, in connection with the transaction contemplated herein.

ARTICLE 9
INTELLECTUAL PROPERTY

9.1 Ownership of Intellectual Property.

9.1.1 Ownership of Background Intellectual Property. As between the Parties, (a) BicycleTx shall own all right, title, and interest in and to any and all BicycleTx Background Patents and BicycleTx Background Know-How, and (b) Genentech shall own all right, title, and interest in and to any and all Genentech Background Patents and Genentech Background Know-How.

9.1.2 Collaboration Inventions.

(a) Sole Ownership. As between the Parties, (i) BicycleTx shall own all right, title, and interest in and to any and all BicycleTx Platform Know-How, BicycleTx Platform Patents, BicycleTx Collaboration Know-How and BicycleTx Collaboration Patents (including all BicycleTx Product Inventions, BicycleTx Product Know-How, and BicycleTx Product Patents) and (ii) Genentech or an Affiliate designated by Genentech shall own all right, title, and interest in and to any and all Genentech Collaboration Know-How and Genentech Collaboration Patents (including all Genentech Product Inventions, Genentech Product Know-How, and Genentech Product Patents).

(b) Joint Ownership. The Parties shall jointly own all Joint Collaboration Inventions. Each Party shall own an equal, undivided interest in any and all Joint Collaboration Inventions, Joint Collaboration Know-How and Joint Collaboration Patents. Subject to the licenses granted under Section 7.1 and Section 7.2, and BicycleTx's Exclusivity Obligations hereunder, each Party shall have the right to Exploit the Joint Collaboration Patents and Joint Collaboration Know-How without a duty of seeking consent from or accounting to the other Party.

9.2 United States Law. The determination of whether an Invention is discovered, made, conceived or reduced to practice by a Party for the purpose of allocating proprietary rights (including Patent, copyright or other intellectual property rights) therein, shall, for purposes of this Agreement, be made in accordance with Applicable Law in the United States.

9.3 Assignment Obligation.

(a) Each Party shall cause all Persons who perform activities for such Party under this Agreement to be under an obligation to assign (or, if such Party is unable to cause such Person to agree to such assignment obligation despite such Party's using commercially reasonable efforts to negotiate such assignment obligation, provide a license under) their rights in any information and inventions

resulting therefrom to such Party, except where Applicable Law requires otherwise and except in the case of governmental, not-for-profit and public institutions which have standard policies against such an assignment (in which case a suitable license, or right to obtain such a license, shall be obtained).

(b) Genentech will promptly disclose to BicycleTx in writing any Platform Inventions, any BicycleTx Platform Know-How, Collaboration Know-How, Collaboration Inventions, Product Know-How and Product Inventions made by Persons (other than BicycleTx) who perform activities for Genentech under this Agreement. Genentech, for itself and on behalf of its Affiliates, hereby assigns (and to the extent such assignment can only be made in the future, hereby agrees to assign) to BicycleTx all of its right, title and interest in and to any and all Platform Inventions (and any BicycleTx Platform Know-How and BicycleTx Platform Patents relating thereto). Genentech will execute and record assignments and other necessary documents consistent with such ownership promptly upon request.

(c) BicycleTx will promptly disclose to Genentech in writing, any Collaboration Know-How, Collaboration Inventions, Product Know-How and Product Inventions made by Persons who perform activities for BicycleTx under this Agreement.

(d) Each Party will promptly disclose to the other Party, in writing, the conception, discovery, development, generation, making or creation of any Joint Collaboration Know-How or Joint Collaboration Inventions made by Persons who perform activities for it under this Agreement. Each Party will execute and record assignments and other necessary documents consistent with such ownership promptly upon request.

9.4 Patent Prosecution and Maintenance.

9.4.1 BicycleTx Background Patents and BicycleTx Platform Patents. BicycleTx shall have the sole right, but not the obligation, through the use of internal or outside counsel of its choice, to prepare, file, prosecute, and maintain the BicycleTx Background Patents and BicycleTx Platform Patents worldwide, at BicycleTx's sole cost and expense.

(a) After Dev Go for a given Collaboration Program, BicycleTx shall keep Genentech reasonably informed regarding each BicycleTx Background Patent or BicycleTx Platform Patent that (a) includes claims that relate to use of the BicycleTx Platform in connection with the Compound(s) for such Collaboration Program; and/or (b) Covers any Compound or Licensed Product (but which Patent falls outside the scope of Product Patents).

(b) The Parties will reasonably cooperate to [***] ("**BicycleTx Other Constructs**"). On a Collaboration Target-by-Collaboration Target basis, after completion of the Lead Generation Phase for a Collaboration Target, BicycleTx shall [***] BicycleTx Other Constructs. Notwithstanding anything herein to the contrary, on a Collaboration Target-by-Collaboration Target basis, if any Patents are filed by or on behalf of BicycleTx after completion of the Lead Generation Phase for a Collaboration Target [***], such Patents shall [***]. On a Collaboration Target-by-Collaboration Target basis, if any BicycleTx Background Patents or BicycleTx Platform Patents exist prior to the delivery of the LSR Go Data Package for a Collaboration Target [***]

[***] BicycleTx Other Constructs, BicycleTx [***] that (i) are [***] and/or (ii) [***] under this Agreement. For clarity, [***]. All remaining Patents in the relevant Patent family shall be included as BicycleTx Collaboration Patents for all purposes in the Agreement, including with respect to all prosecution, enforcement, extension, and other related provisions.

9.4.2 BicycleTx Collaboration Patents. BicycleTx shall (a) prior to Dev Go for a Collaboration Program, have the obligation to prepare, file, prosecute, and maintain the applicable BicycleTx Product Patents [***]; and (b) use good faith efforts to prepare, file, prosecute, and maintain the BicycleTx Collaboration Patents other than BicycleTx Product Patents [***] in a manner consistent with BicycleTx's standard practices with respect to its other Patents. Except as set forth under Section 9.4.5 with respect to BicycleTx Product Patents following Dev Go for a given Collaboration Program, in consultation with Genentech, BicycleTx shall have the sole right, through the use of internal counsel, or outside counsel [***], to prepare, file, prosecute, and maintain the BicycleTx Collaboration Patents worldwide, at BicycleTx's sole cost and expense. BicycleTx shall keep Genentech fully informed of all material steps with regard to the preparation, filing, prosecution, and maintenance of all BicycleTx Collaboration Patents, [***]. BicycleTx shall [***] the requests and suggestions of Genentech with respect to such BicycleTx drafts and with respect to strategies for filing and prosecuting the BicycleTx Collaboration Patents in the Territory. Notwithstanding the foregoing, BicycleTx shall promptly inform Genentech of any adversarial patent office proceeding or *sua sponte* filing, including a request for, or filing of or declaration of, any interference, opposition, Third Party observation, derivation proceeding, *inter partes* review, post grant review, supplementary examination, reissue or inter parte or ex parte reexamination relating to a BicycleTx Collaboration Patent in the Territory. The Parties shall thereafter consult and cooperate to determine a course of action with respect to any such proceeding in the Territory and BicycleTx shall [***] all comments, requests and suggestions provided by Genentech. BicycleTx shall not [***]. If BicycleTx decides not to prepare, file, prosecute, or maintain any BicycleTx Collaboration Patent other than a BicycleTx Product Patent [***], BicycleTx shall provide reasonable prior written notice to Genentech of such intention (which notice shall, in any event, be given no later than [***] prior to the next deadline for any action that may be taken with respect to such BicycleTx Collaboration Patent other than a BicycleTx Product Patent [***]), and Genentech may thereupon provide BicycleTx written notice to elect for BicycleTx to continue the preparation, filing, prosecution, and maintenance of such BicycleTx Collaboration Patent other than a BicycleTx Product Patent [***], at Genentech's sole cost and expense. Upon BicycleTx's receipt of such written notice, BicycleTx shall

continue the preparation, filing, prosecution, and maintenance of such BicycleTx Collaboration Patent other than a BicycleTx Product Patent [***], at Genentech's sole cost and expense.

9.4.3 Genentech Background Patents. Genentech shall have the sole right, but not the obligation, through the use of internal or outside counsel, to prepare, file, prosecute, and maintain the Genentech Background Patents worldwide, at Genentech's sole cost and expense.

9.4.4 Genentech Collaboration Patents and Joint Collaboration Patents. Genentech shall have the first right, but not the obligation, through the use of internal counsel, or outside counsel reasonably acceptable to BicycleTx, to prepare, file, prosecute, and maintain the Genentech Collaboration Patents and Joint Collaboration Patents worldwide, at Genentech's sole cost and expense. Genentech shall keep BicycleTx fully informed of all material steps with regard to the preparation, filing, prosecution, and maintenance of Genentech Collaboration Patents and Joint Collaboration Patents, [***]. Genentech shall [***] the requests and suggestions of BicycleTx with respect to such Genentech drafts and with respect to strategies for filing and prosecuting the Genentech Collaboration Patents and Joint Collaboration Patents in the Territory. If Genentech decides not to prepare, file, prosecute, or maintain a Genentech Collaboration Patent or Joint Collaboration Patent in a country or other jurisdiction in the Territory, Genentech shall provide reasonable prior written notice to BicycleTx of such intention (which notice shall, in any event, be given no later than [***] prior to the next deadline for any action that may be taken with respect to such Genentech Collaboration Patent or Joint Collaboration Patent in such country or other jurisdiction), and BicycleTx shall thereupon have the option, in its sole discretion, to assume the control and direction of the preparation, filing, prosecution, and maintenance of such Genentech Collaboration Patent or Joint Collaboration Patent at its sole cost and expense in such country or other jurisdiction. Upon BicycleTx's written acceptance of such option, BicycleTx shall assume the responsibility and control for the preparation, filing, prosecution, and maintenance of such Genentech Collaboration Patent or Joint Collaboration Patent. In such event, Genentech shall reasonably cooperate with BicycleTx with respect to such Genentech Collaboration Patent or Joint Collaboration Patent in such country or other jurisdiction as provided under Section 9.4.6.

9.4.5 Product Patents Following Dev Go. On a Collaboration Program-by-Collaboration Program basis, Genentech shall have the first right, but not the obligation, through the use of internal counsel, or outside counsel [***], to prepare, file, prosecute, and maintain (a) the Genentech Product Patents, and (b) following Dev Go for a given Collaboration Program, all BicycleTx Product Patents arising from such Collaboration Program, on a worldwide basis, at Genentech's sole cost and expense. Upon Genentech's request following the delivery by Genentech of a Dev Go Notice for a given Collaboration Program, BicycleTx shall promptly take all necessary steps to transfer to Genentech's selected patent counsel the prosecution files and materials for all BicycleTx Product Patents specifically relating to such Collaboration Program. Genentech shall keep BicycleTx fully informed of all material steps with regard to the preparation, filing, prosecution, and maintenance of Product Patents, [***]

[***]. Genentech shall [***] the requests and suggestions of BicycleTx with respect to such Genentech drafts and with respect to strategies for filing and prosecuting the Product Patents in the Territory. If Genentech decides not to prepare, file, prosecute, or maintain a Product Patent in a country or other jurisdiction in the Territory, Genentech shall provide reasonable prior written notice to BicycleTx of such intention (which notice shall, in any event, be given no later than [***] prior to the next deadline for any action that may be taken with respect to such Product Patent in such country or other jurisdiction), and BicycleTx shall thereupon have the option, in its sole discretion, to assume the control and direction of the preparation, filing, prosecution, and maintenance of such Product Patent at its sole cost and expense in such country or other jurisdiction. Upon BicycleTx's written acceptance of such option, BicycleTx shall assume the responsibility and control for the preparation, filing, prosecution, and maintenance of such specific Product Patent. In such event, Genentech shall reasonably cooperate with BicycleTx with respect to such Product Patent in such country or other jurisdiction as provided under Section 9.4.6.

9.4.6 Cooperation. The Parties agree to cooperate fully in the preparation, filing, prosecution, and maintenance of the Product Patents and Collaboration Patents in the Territory under this Agreement. Cooperation shall include:

(a) without limiting any other rights and obligations of the Parties under this Agreement, cooperating with respect to the timing, scope and filing of such Patents to preserve and enhance the patent protection for Compounds and Licensed Products, including the manufacture and use thereof;

(b) executing all papers and instruments, or requiring its employees or contractors to execute such papers and instruments, so as to (i) effectuate the ownership of intellectual property set forth in Section 9.1.1 and Section 9.1.2; (ii) enable the other Party to apply for and to prosecute Patent applications in the Territory; and (iii) obtain and maintain any Patent extensions, supplementary protection certificates, and the like with respect to the Product Patents and Collaboration Patents in the Territory, in each case ((i), (ii), and (iii)) to the extent provided for in this Agreement;

(c) consistent with this Agreement, assisting in any license registration processes with applicable governmental authorities that may be available in the Territory for the protection of a Party's interests in this Agreement; and

(d) promptly informing the other Party of any matters coming to such Party's attention that may materially affect the preparation, filing, prosecution, or maintenance of any such Patents in the Territory.

9.4.7 CREATE Act. It is the intention of the Parties that this Agreement is a "joint research agreement" as that phrase is defined in 35 USC § 102(c) (AIA) or 35 USC § 103(c) (pre-AIA). In the event that either Party to this Agreement intends to overcome a rejection of a claimed invention within the Collaboration Patents or Product Patents under this Agreement pursuant to the provisions of 35 USC § 102(c) or 35 USC § 103(c), such Party shall first obtain the prior written consent of the other Party. Following receipt of such written consent, such Party shall limit any amendment to the specification or statement to the patent office with respect to this Agreement to that which is strictly required by 35 USC § 102(c) or 35 USC § 103(c) and the rules and regulations promulgated thereunder and which is consistent with the terms and conditions of this Agreement. If the Parties agree that, in order to overcome a rejection of a claimed invention within the Collaboration Patents and/or Product Patents pursuant to the provisions of the CREATE Act, the filing of a terminal disclaimer is required or advisable, the Parties shall first agree

on terms and conditions under which the patent application subject to such terminal disclaimer and the patent or application over which such application is disclaimed shall be jointly enforced, if and to the extent that the Parties have not previously agreed to such terms and conditions. If Genentech enters into an agreement with a Third Party with respect to the further research, development or commercialization of a Compound, a Development Candidate or Licensed Product, BicycleTx shall, upon Genentech's request, similarly enter into such agreement with such Third Party for the purposes of furthering the Parties' objectives under this Agreement, provided that such agreement is consistent with the rights of BicycleTx under this Section 9.4.7 and does not place any material obligation on BicycleTx.

9.4.8 Patent Term Extension and Supplementary Protection Certificate. Genentech shall be responsible for making decisions regarding patent term extensions, including supplementary protection certificates and any other extensions that are now or become available in the future, wherever applicable, for Genentech Background Patents, Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents in any country or other jurisdiction and for applying for any extension or supplementary protection certificate with respect to such Patents in the Territory. BicycleTx shall provide prompt and reasonable assistance, as requested by Genentech, including by taking such action as patent holder as is required under any Applicable Law to obtain such patent extension or supplementary protection certificate. Genentech shall pay all expenses with respect to obtaining the extension or supplementary protection certificate in the Territory. In case that Genentech desires that a patent term extension should be applied for a BicycleTx Platform Patent or a BicycleTx Background Patent, BicycleTx and Genentech shall [***], provided that [***].

9.4.9 Patent Listings. Genentech will have the sole right to make all filings with Regulatory Authorities in the Territory with respect to Genentech Background Patents, Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents, including as required or allowed under Applicable Law, provided that with respect to Joint Collaboration Patents such right shall be solely with respect to Licensed Products. Genentech shall notify BicycleTx in writing of any BicycleTx Background Patents and BicycleTx Platform Patents that it intends to list with Regulatory Authorities related to the Licensed Products and, prior to filing any such listing, consult with and [***] the requests and suggestions of BicycleTx regarding the same.

9.5 Patent Enforcement.

9.5.1 BicycleTx Background Patents, BicycleTx Platform Patents and BicycleTx Collaboration Patents.

(a) Each Party shall promptly notify the other Party in writing of any alleged or threatened infringement of a BicycleTx Background Patent or BicycleTx Collaboration Patent by a Third Party in the Territory of which such Party becomes aware based on the development, commercialization, or an application to market a product containing a Compound or any Licensed Product in the Territory (the "**Product Infringement**").

(b) BicycleTx shall have the sole right, but not the obligation, to prosecute any Product Infringement involving any claims of BicycleTx Background Patents, BicycleTx Platform Patents and BicycleTx Collaboration Patents at its sole expense and BicycleTx shall retain control of the prosecution of such claim, suit or proceeding.

9.5.2 Genentech Background Patents, Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents.

(a) Each Party shall promptly notify the other Party in writing of any alleged or threatened infringement of a Genentech Background Patent, Genentech Collaboration Patent, a Product Patent or a Joint Collaboration Patent by a Third Party in the Territory of which such Party becomes aware (including alleged or threatened infringement based on the development, commercialization, or an application to market a product containing a Compound or any Licensed Product in the Territory).

(b) Genentech shall have the sole right, but not the obligation, to prosecute any such infringement of Genentech Background Patents in the Territory at its sole expense, and Genentech shall retain control of the prosecution of such claim, suit or proceeding.

(c) Genentech shall have the first right, but not the obligation, to prosecute any such infringement of Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents, in each case in the Territory at its sole expense, and Genentech shall retain control of the prosecution of such claim, suit or proceeding. In the event Genentech prosecutes any such infringement, BicycleTx shall have the right to join as a party to such claim, suit or proceeding in the Territory and participate with its own counsel at its own expense; provided that Genentech shall retain control of the prosecution of such claim, suit or proceeding. If Genentech does not take commercially reasonable steps to prosecute the alleged or threatened infringement in the Territory with respect to any such Genentech Collaboration Patent, Product Patent or Joint Collaboration Patent (i) within [***] following the first notice provided above with respect to such alleged infringement, or (ii) [***] before the time limit, if any, set forth in appropriate laws and regulations for filing of such actions, whichever comes first, then BicycleTx may prosecute the alleged or threatened infringement in the Territory at its own expense.

9.5.3 Cooperation. The Parties agree to cooperate fully in any infringement action pursuant to this Section 9.5. To the extent necessary for a Party to bring such an action, the other Party shall, where necessary, furnish a power of attorney solely for such purpose or shall join in, or be named as a necessary party to, such action. Unless otherwise set forth herein, the Party entitled to bring any patent infringement litigation in accordance with this Section 9.5 shall have the right to settle such claim; provided that neither Party shall have the right to settle any patent infringement litigation under this Section 9.5 in a manner that materially diminishes or has a material adverse effect on the rights or interest of the other Party, or in a manner that imposes any costs or liability on, or involves any admission by, the other Party, without the express written consent of such other Party. The Party commencing the litigation shall provide the other Party with copies of all pleadings and other documents filed with the court and shall consider reasonable input from the other Party during the course of the proceedings.

9.5.4 Recovery. Any recovery realized as a result of such litigation described in Section 9.5.1 or Section 9.5.2 (whether by way of settlement or otherwise) shall be first allocated to reimburse the Parties for their costs and expenses in making such recovery (which amounts shall be allocated pro rata if insufficient to cover the totality of such expenses). Any remainder after such reimbursement is made shall be [***]; provided, that [***].

9.6 Infringement Claims by Third Parties. If the manufacture, sale, or use of a Discovery Construct or Licensed Product in the Territory pursuant to this Agreement results in, or may result in, any claim, suit, or proceeding by a Third Party alleging patent infringement by Genentech (or its Affiliates or Sublicensees), Genentech shall promptly notify BicycleTx thereof in writing. Genentech shall have the first right, but not the obligation, to defend and control the defense of any such claim, suit, or proceeding at its own expense, using counsel of its own choice. BicycleTx may participate in any such claim, suit, or proceeding with counsel of its choice at its own expense. Without limitation of the foregoing, if Genentech finds it necessary or desirable to join BicycleTx as a party to any such action, BicycleTx shall, at Genentech's expense, execute all papers and perform such acts as shall be reasonably required. If Genentech elects (in a written communication submitted to BicycleTx within a reasonable amount of time after notice of the alleged patent infringement) not to defend or control the defense of, or otherwise fails to initiate and maintain the defense of, any such claim, suit, or proceeding, within such time periods so that BicycleTx is not prejudiced by any delays, BicycleTx may conduct and control the defense of any such claim, suit, or proceeding at its own expense. Each Party shall keep the other Party reasonably informed of all material developments in connection with any such claim, suit, or proceeding. Any recoveries by Genentech of any sanctions awarded to Genentech and against a party asserting a claim being defended under this Section 9.6 shall be applied first to reimburse each Party for its reasonable out-of-pocket costs of defending or participating in such claim, suit, or proceedings, on a pro rata basis. The balance of any such recoveries shall be [***].

9.7 Invalidity or Unenforceability Defenses or Actions.

9.7.1 Notice. Each Party shall promptly notify the other Party in writing of any alleged or threatened assertion of invalidity or unenforceability of any of the BicycleTx Background Patents, BicycleTx Platform Patents, Genentech Background Patents, Genentech Collaboration Patents, Product Patents or Joint Collaboration Patents by a Third Party, in each case in the Territory and of which such Party becomes aware.

9.7.2 BicycleTx Background Patents. BicycleTx shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the BicycleTx Background Patents at its own expense in the Territory.

9.7.3 BicycleTx Platform Patents and BicycleTx Collaboration Patents. Subject to Section 9.7.5 with respect to BicycleTx Product Patents following Dev Go for a given Collaboration Program, BicycleTx shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the BicycleTx Platform Patents and BicycleTx Collaboration Patents at its own expense in the Territory. Genentech may participate in any such claim, suit, or proceeding in the Territory with counsel of its choice at its own expense; provided that BicycleTx shall retain control of the defense in such claim, suit, or proceeding.

9.7.4 Genentech Background Patents. Genentech shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the Genentech Background Patents at its own expense in the Territory.

9.7.5 Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents. Genentech shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the Genentech Collaboration Patents, Product Patents and Joint

Collaboration Patents at its own expense in the Territory, provided that with respect to BicycleTx Product Patents, Genentech shall have such rights only following Dev Go for the applicable Collaboration Program. BicycleTx may participate in any such claim, suit, or proceeding in the Territory related to the Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents with counsel of its choice at its own expense; provided that Genentech shall retain control of the defense in such claim, suit, or proceeding. If Genentech elects not to defend or control the defense of the Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents in a suit brought in the Territory, or otherwise fails to initiate and maintain the defense of any such claim, suit, or proceeding, then BicycleTx may conduct and control the defense of any such claim, suit, or proceeding, at its own expense; provided, that BicycleTx shall obtain the written consent of Genentech prior to settling or compromising such defense.

9.7.6 Cooperation. Each Party shall assist and cooperate with the other Party as such other Party may reasonably request from time to time in connection with its activities set forth in this Section 9.7, including by being joined as a party plaintiff in such action or proceeding, providing access to relevant documents and other evidence, and making its employees available at reasonable business hours. In connection with any such defense or claim or counterclaim, the controlling Party shall consider in good faith any comments from the other Party, shall keep the other Party reasonably informed of any steps taken, and shall provide copies of all documents filed, in connection with such defense, claim, or counterclaim. In connection with the activities set forth in this Section 9.7, each Party shall consult with the other as to the strategy for the defense of the BicycleTx Collaboration Patents, Genentech Collaboration Patents, Product Patents and Joint Collaboration Patents.

9.8 Third Party Licenses. If, [***], the Development, Manufacture, or Commercialization of any Compound or Licensed Product by Genentech, any of its Affiliates, or any of its or their Sublicensees would infringe or misappropriate any Patent, trade secret, or other intellectual property right of a Third Party in any country or other jurisdiction in the Territory, then Genentech shall have the sole right, but not the obligation, to negotiate and obtain a license from such Third Party [***] for Genentech and its Affiliates, and its and their Sublicensees to Develop, Manufacture, and Commercialize a Compound or Licensed Products in such country or other jurisdiction, and Genentech shall promptly provide BicycleTx with written notice of any such license, including the identity of the counter-party and a description of the Patent, trade secret, or other intellectual property right. For clarity, BicycleTx shall be solely responsible for obtaining, negotiating, maintaining BicycleTx Future In-License Agreements and paying any payments due under such BicycleTx Future In-License Agreements. Notwithstanding the foregoing, any Know-How, Regulatory Documentation, material, Patent, or other property right to which rights are obtained by BicycleTx under any agreement entered into following the Effective Date other than a BicycleTx Future In-License Agreement (collectively, "**Future Rights**"), and for which payments are or would be owed to a Third Party for the Exploitation of such Future Rights in connection with a Compound or Licensed Product under this Agreement, shall not be deemed to be included within BicycleTx Background Patents or BicycleTx Background Know-How, or within the license granted to Genentech pursuant to Section 7.1, unless [***].

9.9 Product Trademarks. As between the Parties, Genentech shall own all right, title, and interest to the Product Trademarks in the Territory, and shall be responsible for the registration, prosecution, maintenance and enforcement thereof. All costs and expenses of registering, prosecuting, maintaining and enforcing the Product Trademarks shall be borne solely by Genentech. BicycleTx shall provide all

assistance and documents reasonably requested by Genentech in support of its prosecution, registration, maintenance and enforcement of the Product Trademarks.

9.10 Inventor's Remuneration. Each Party shall be solely responsible for any remuneration that may be due such Party's inventors under any applicable inventor remuneration laws.

9.11 Common Interest. All information exchanged between the Parties regarding the prosecution, maintenance, enforcement and defense of Patents under this ARTICLE 9 will be deemed to be Confidential Information of the disclosing Party. In addition, the Parties acknowledge and agree that, with regard to such prosecution, maintenance, enforcement and defense, the interests of the Parties as collaborators are to, for their mutual benefit, obtain patent protection and plan patent defense against potential infringement activities by Third Parties, and as such, are aligned and are legal in nature. The Parties agree and acknowledge that they have not waived, and nothing in this Agreement constitutes a waiver of, any legal privilege concerning Patents under this ARTICLE 9, including privilege under the common interest doctrine and similar or related doctrines. Notwithstanding anything to the contrary in this Agreement, to the extent a Party has a good faith belief that any information required to be disclosed by such Party to the other Party under this ARTICLE 9 is protected by attorney-client privilege or any other applicable legal privilege or immunity, such Party shall not be required to disclose such information and the Parties shall in good faith cooperate to agree upon a procedure (including without limitation entering into a specific common interest agreement or disclosing such information on a "for counsel eyes only" basis or similar procedure) under which such information may be disclosed without waiving or breaching such privilege or immunity.

ARTICLE 10
PHARMACOVIGILANCE AND SAFETY

10.1 Pharmacovigilance. On a Licensed Product-by-Licensed Product basis, the Parties shall determine the necessity and timing for the execution of a separate pharmacovigilance agreement specifying the procedure for the information exchange of safety data and adverse events that may occur during the clinical Development of a Licensed Product. Each such pharmacovigilance agreement shall be in a mutually agreed format and enable each Party to meet reporting requirements with any applicable Regulatory Authority and include the set-up and maintenance of a global safety database.

10.2 Notification requirements. During the Term, BicycleTx shall promptly notify Genentech of any safety issues of which BicycleTx becomes aware that [***].

ARTICLE 11
CONFIDENTIALITY AND NON-DISCLOSURE

11.1 Confidentiality Obligations. At all times during the Term and for a period of [***] following termination or expiration hereof in its entirety, each Party shall, and shall cause its officers, directors, employees and agents to, keep confidential and not publish or otherwise disclose to a Third Party and not use, directly or indirectly, for any purpose, any Confidential Information furnished or otherwise made known to it, directly or indirectly, by the other Party, except to the extent such disclosure or use is expressly permitted by the terms of this Agreement or is reasonably necessary or useful for the performance of, or the exercise of such Party's rights under, this Agreement. Notwithstanding the foregoing, to the extent the receiving Party can demonstrate by documentation or other competent proof, the confidentiality and non-use obligations under this Section 11.1 with respect to any Confidential Information shall not include any information that:

11.1.1 has been published by a Third Party or otherwise is or hereafter becomes part of the public domain by public use, publication, general knowledge or the like through no wrongful act, fault or negligence on the part of the receiving Party;

11.1.2 has been in the receiving Party's possession prior to disclosure by the disclosing Party without any obligation of confidentiality with respect to such information; provided that the foregoing exception shall not apply to Joint Know-How;

11.1.3 is subsequently received by the receiving Party from a Third Party without restriction and without breach of any agreement between such Third Party and the disclosing Party;

11.1.4 is generally made available to Third Parties by the disclosing Party without restriction on disclosure; or

11.1.5 has been independently developed by or for the receiving Party without reference to, or use or disclosure of, the disclosing Party's Confidential Information; provided that the foregoing exception shall not apply to Joint Know-How.

Specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the receiving Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination and its principles are in the public domain or in the possession of the receiving Party.

11.2 Permitted Use or Disclosures.

11.2.1 Each Party may disclose Confidential Information to the extent that such disclosure is, in the reasonable opinion of the receiving Party's legal counsel, required to be disclosed pursuant to law, regulation or a valid order of a court of competent jurisdiction or other supra-national, federal, national, regional, state, provincial or local governmental body of competent jurisdiction provided, that the receiving Party shall first have given prompt written notice (and to the extent possible, at least [***] notice) to the disclosing Party and given the disclosing Party a reasonable opportunity to take whatever action it deems necessary to protect its Confidential Information. If no protective order or other remedy is obtained, or the disclosing Party waives compliance with the terms of this Agreement, the receiving Party shall furnish only that portion of Confidential Information which the receiving Party is advised by counsel is legally required to be disclosed; for clarity, disclosures required in the reasonable opinion of the receiving Party's legal counsel to the U.S. Securities and Exchange Commission (or equivalent foreign agency) shall be subject to the following Section 11.2.2.

11.2.2 The Parties acknowledge that either or both Parties (or its Affiliates) may be obligated to make one or more filings (including to file a copy of this Agreement) with the U.S. Securities and Exchange Commission (or equivalent foreign agency) or a governmental authority. Each Party will be entitled to make such a required filing, provided that if such filing includes a copy of this Agreement it will (a) submit in connection with such filing a copy of this Agreement in a form mutually agreed by the Parties in advance or, if, despite the reasonable efforts of BicycleTx, a form mutually agreed by the Parties cannot be agreed in advance, redacted to the extent permitted by Applicable Law (the "**Redacted Agreement**"), (b) request, and use reasonable efforts consistent with Applicable Laws to obtain confidential treatment of

all terms redacted from this Agreement, as reflected in the Redacted Agreement, [***], (c) to the extent consistent with Applicable Law, promptly deliver to the other Party any written correspondence received by it or its representatives from the U.S. Securities and Exchange Commission (or equivalent foreign agency) or a governmental authority with respect to such confidential treatment request and promptly advise the other Party of any other material communications between it or its representatives with the U.S. Securities and Exchange Commission (or equivalent foreign agency) or a governmental authority with respect to such confidential treatment request, (d) upon the written request of the other Party, if legally justifiable, request an appropriate extension of the term of the confidential treatment period, and (e) if [***] in the Redacted Agreement, use reasonable efforts [***]. For clarity, following a request from a governmental authority to change the redactions requested by a Party, [***] such Party shall provide the other Party with a notice of the required change and a copy of the revised redactions. Each Party will be responsible for its own legal and other external costs in connection with any such filing, registration or notification.

11.2.3 Each Party may disclose the terms and conditions of this Agreement and Confidential Information of the other Party (a) on a need-to-know basis to its legal and financial advisors under appropriate conditions of confidentiality, (b) under appropriate conditions of confidentiality in connection with an actual or potential (i) permitted license or sublicense of its rights hereunder, (ii) debt, lease or equity financing of such Party, (iii) merger, Acquisition, consolidation, share exchange or other similar transaction involving such Party and a Third Party, or (iv) co-funding or financing arrangement, provided that in each (i) to (iv) the receiving Party provides prior written notice of such disclosure to the disclosing Party and, to the extent practicable, takes reasonable and lawful actions to minimize the degree of such disclosure, (c) to any Third Party that is or may be engaged to perform services in connection with the Development, Manufacturing, or Commercialization of the Products as necessary to enable such Third Party to perform such services and under appropriate conditions of confidentiality, (d) to any government agency or authority in connection with seeking government, funding, support or grants, and (e) to the extent such disclosure is reasonably necessary in filing, prosecuting, or enforcing patent, copyright and trademark rights, obtaining and maintaining Regulatory Approvals, or conducting preclinical or clinical trials and (f) to Third Parties requesting clinical trial data information (in accordance with the then-current data sharing policy of Genentech and its Affiliates; provided that prior to any such disclosures pursuant to (a)-(c), any Third Party receiving such Confidential Information of the disclosing Party shall be contractually obligated to substantially the same obligations of non-disclosure and non-use of the receiving Party as set forth in Section 11.1, and the receiving Party shall be liable for any breach thereof by such Third Party.

11.3 Use of Name. Except as expressly provided herein, neither Party shall mention or otherwise use the name, logo, or Trademark of the other Party or any of its Affiliates (or any abbreviation or adaptation thereof) in any publication, press release, marketing and promotional material, or other form of publicity without the prior written approval of such other Party in each instance. The restrictions imposed by this Section 11.3 shall not prohibit either Party from making any disclosure identifying the other Party that, in the opinion of the disclosing Party's counsel, is required by Applicable Law; provided, that such Party shall submit the proposed disclosure identifying the other Party in writing to the other Party as far in

advance as reasonably practicable (and in no event less than [***] prior to the anticipated date of disclosure) so as to provide a reasonable opportunity to comment thereon.

11.4 Press Releases. Genentech shall issue press releases in accordance with its internal policy that typically does not issue a second press release until clinical proof of concept has been achieved for a Licensed Product. Genentech shall provide BicycleTx with a copy of any draft press release related to the activities contemplated by this Agreement at least [***] (or such shorter period as may be mandated by Applicable Law) prior to its intended publication for BicycleTx's review. [***]. Genentech shall consider BicycleTx's suggestions in issuing its press release. BicycleTx shall only issue press releases related to the activities contemplated by this Agreement that either [***]. In all circumstances, BicycleTx shall provide Genentech with a draft press release at least [***] (or such shorter period as may be mandated by Applicable Law) prior to its intended publication for Genentech's review. During such period, Genentech shall [***]. To ensure communication alignment, responses (if any) to inquiries by media or other Third Parties after issuance of a permitted press release by BicycleTx (solely or jointly with Genentech) shall consist solely of the press release language or shall follow the response guidelines that may be mutually developed by the Parties.

11.5 Publications. During the Term, the following restrictions shall apply with respect to disclosure by any Party of Confidential Information relating to the Licensed Product in any publication or presentation:

11.5.1 Both Parties acknowledge that it is their policy for the studies and results thereof to be registered and published in accordance with their internal guidelines. Genentech, in accordance with its internal policies and procedures, shall have the right to publish all studies and clinical trials conducted by or on behalf of Genentech (and results thereof) on the clinical trial registries that are maintained by or on behalf of Genentech without BicycleTx's review or approval if no Confidential Information of BicycleTx is included. BicycleTx shall not publish any studies, clinical trials or results thereof related to this Agreement on its clinical trial registry, provided however, that Genentech's clinical trial registry can be accessed via a link from Bicycle's clinical trial registry.

11.5.2 A Party ("**Publishing Party**") shall provide the other Party with a copy of any proposed publication or presentation at least [***] prior to submission for publication so as to provide such other Party with an opportunity to recommend any changes to the Publishing Party that it reasonably believes are necessary to continue to maintain such Party's Confidential Information in accordance with the requirements of this Agreement. The incorporation of such recommended changes shall not be unreasonably refused; and if such other Party notifies ("**Publishing Notice**") the Publishing Party in writing, within [***] after receipt of the copy of the proposed publication or presentation, that such publication or presentation in its reasonable judgment (a) contains an Invention, solely or jointly conceived and/or reduced to practice by the other Party, for which the other Party reasonably desires to obtain patent protection or (b) could be expected to have a material adverse effect on the commercial value of any Confidential Information disclosed by the other Party to the Publishing Party, the Publishing Party

shall prevent such publication or delay such publication for a mutually agreeable period of time. In the case of Inventions, a delay shall be for a period reasonably sufficient to permit the timely preparation and filing of a patent application(s) on such invention, and in no event less than [***] from the date of the Publishing Notice. Notwithstanding anything to the contrary in this Section 11.5.2, [***].

11.6 Destruction of Confidential Information. Upon the effective date of the termination of this Agreement for any reason, the Parties shall, with respect to Confidential Information (in the event of termination of this Agreement with respect to one (1) or more Terminated Territories or Terminated Targets but not in its entirety, solely to the extent relating specifically and exclusively to such Terminated Territories and/or Terminated Targets or Terminated Assets, as applicable) to which such other Party does not retain rights under the surviving provisions of this Agreement, as soon as reasonably practicable, destroy all copies of such Confidential Information in the possession of the other Party and confirm such destruction in writing to the other Party, provided, that such other Party shall be permitted to retain one (1) copy of such Confidential Information for the sole purpose of performing any continuing obligations hereunder, as required by Applicable Law, or for archival purposes. [***] Notwithstanding the foregoing, such other Party also shall be permitted to retain such additional copies of or any computer records or files containing such Confidential Information that have been created solely by such Party's automatic archiving and back-up procedures, to the extent created and retained in a manner consistent with such other Party's standard archiving and back-up procedures, but not for any other use or purpose.

ARTICLE 12
REPRESENTATIONS AND WARRANTIES

12.1 Mutual Representations and Warranties. BicycleTx and Genentech each represents and warrants to the other, as of the Effective Date, as follows:

12.1.1 Organization. It is a corporation duly incorporated, validly existing, and in good standing under the laws of the jurisdiction of its incorporation, and has all requisite corporate power and authority, to execute, deliver, and perform this Agreement.

12.1.2 Authorization. The execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action and do not violate (a) such Party's charter documents, bylaws, or other organizational documents, (b) in any material respect, any agreement, instrument, or contractual obligation to which such Party is bound, (c) any requirement of any Applicable Law, or (d) any order, writ, judgment, injunction, decree, determination, or award of any court or governmental agency presently in effect applicable to such Party.

12.1.3 Binding Agreement. This Agreement is a legal, valid, and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights,

judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity).

12.1.4 No Inconsistent Obligation. It is not under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement or that would impede the diligent and complete fulfillment of its obligations hereunder.

12.2 Additional Representations and Warranties of Bicycle. BicycleTx further represents and warrants to Genentech, as of the Effective Date, as follows:

12.2.1 All BicycleTx Background Patents and BicycleTx Platform Patents existing as of the Effective Date are listed on Schedule 12.2.1 (the "**Existing Patents**").

12.2.2 There are no judgments, or settlements against, or amounts with respect thereto, owed by BicycleTx or any of its Affiliates relating to the Existing Patents or the BicycleTx Background Know-How. No claim or litigation has been brought or threatened in writing or any other form by any Person alleging, and BicycleTx has no knowledge of any claim, whether or not asserted, that the Existing Patents are invalid or unenforceable.

12.2.3 To BicycleTx's knowledge, no Person is infringing or threatening to infringe or misappropriating or threatening to misappropriate the Existing Patents or the BicycleTx Background Know-How.

12.2.4 BicycleTx is the sole and exclusive owner of the entire right, title and interest in the Existing Patents, and such Existing Patents are free of any encumbrance, lien, or claim of ownership by any Third Party. BicycleTx is entitled to grant the licenses specified herein.

12.2.5 Neither BicycleTx nor any of its employees nor, to BicycleTx's knowledge, agents performing hereunder, have ever been, are currently, or are the subject of a proceeding that could lead to it or such employees or agents becoming, as applicable, a Debarred Entity or Debarred Individual, an Excluded Entity or Excluded Individual or a Convicted Entity or Convicted Individual or added to the FDA's Disqualified/Restricted List. If, during the Term, BicycleTx, or any of its employees or agents performing hereunder, become or are the subject of a proceeding that could lead to a Person becoming, as applicable, a Debarred Entity or Debarred Individual, an Excluded Entity or Excluded Individual or a Convicted Entity or Convicted Individual or added to the FDA's Disqualified/Restricted List, BicycleTx shall immediately notify Genentech, and Genentech shall have the right, exercisable upon written notice given by Genentech to terminate this Agreement. This provision shall survive termination or expiration of this Agreement. For purposes of this Agreement, the following definitions shall apply:

(a) A "**Debarred Individual**" is an individual who has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from providing services in any capacity to a person that has an approved or pending drug or biological product application.

(b) A "**Debarred Entity**" is a corporation, partnership or association that has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from submitting or assisting in the submission of any Drug Approval Application, or a subsidiary or affiliate of a Debarred Entity.

(c) An "**Excluded Individual**" or "**Excluded Entity**" is (i) an individual or entity, as applicable, who has been excluded, debarred, suspended or is otherwise ineligible to participate

in federal health care programs such as Medicare or Medicaid by the Office of the Inspector General (OIG/HHS) of the U.S. Department of Health and Human Services, or (ii) is an individual or entity, as applicable, who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal procurement and non-procurement programs, including those produced by the U.S. General Services Administration (GSA).

(d) A "**Convicted Individual**" or "**Convicted Entity**" is an individual or entity, as applicable, who has been convicted of a criminal offense that falls within the ambit of 21 U.S.C. §335a (a) or 42 U.S.C. §1320a - 7(a), but has not yet been excluded, debarred, suspended or otherwise declared ineligible.

(e) "**FDA's Disqualified/Restricted List**" is the list of clinical investigators restricted from receiving investigational drugs, biologics, or devices who the FDA has determined have repeatedly or deliberately failed to comply with regulatory requirements for studies or have submitted false information to the study sponsor or the FDA.

12.3 Additional Representations, Warranties and Covenants of Genentech. Genentech represents and warrants to BicycleTx, as of the Effective Date, as follows:

12.3.1 that Genentech is entitled to grant BicycleTx the license as specified in Section 7.2 with regard to Genentech Background Patents and Genentech Background Know-How Controlled by Genentech or any of its Affiliates on the Effective Date.

12.3.2 Genentech covenants to BicycleTx that if it becomes aware that any employee or agent performing activities in connection with a Collaboration Program is, at any time during the conduct of such Collaboration Program, a Debarred Entity or Debarred Individual, an Excluded Entity or Excluded Individual or a Convicted Entity or Convicted Individual or added to the FDA's Disqualified/Restricted List, it shall immediately notify BicycleTx thereof. This provision shall survive termination or expiration of this Agreement.

12.4 Covenants of Bicycle. BicycleTx covenants to Genentech as follows:

12.4.1 During the Term, neither BicycleTx nor any of its Affiliates shall encumber or diminish the rights granted to Genentech hereunder with respect to the BicycleTx Patents, including by not (a) knowingly committing any acts or knowingly permitting the occurrence of any omissions that would adversely affect the rights granted to Genentech hereunder, (b) knowingly committing any acts or knowingly permitting the occurrence of any omissions that would cause the breach or termination of any BicycleTx Future In-License Agreement, or (c) amending or otherwise modifying or permitting to be amended or modified, any BicycleTx Future In-License Agreement, where such amendment or modification would adversely affect the rights granted to Genentech hereunder. BicycleTx shall promptly provide Genentech with notice of any alleged, threatened, or actual breach of any BicycleTx Future In-License Agreement.

12.4.2 In performing obligations under this Agreement, BicycleTx and its Affiliates will not knowingly infringe or misappropriate any Patents or other intellectual property that are Controlled by Third Parties but are not Controlled by BicycleTx or its Affiliates.

12.4.3 BicycleTx and its Affiliates will employ Persons with appropriate education, knowledge and experience to conduct and to oversee the Discovery Research Activities.

12.4.4 BicycleTx shall have obtained from each of its Affiliates, sublicensees, employees and agents who are participating in the Exploitation of the Compounds or Licensed Products or who otherwise have access to any Genentech Know-How or other Confidential Information of Genentech, rights to any and all Know-How that is reasonably necessary for the Development or Commercialization of Compounds or Licensed Products, in each case prior to the performance of or participation in such activities, such that Genentech shall, by virtue of this Agreement, receive from BicycleTx, without payments beyond those required by ARTICLE 8, the licenses and other rights granted to Genentech hereunder.

12.5 DISCLAIMER OF WARRANTIES. EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATIONS OR GRANTS ANY WARRANTIES, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, WHETHER WRITTEN OR ORAL, OR EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF QUALITY, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR USE OR PURPOSE OR ANY WARRANTY AS TO THE VALIDITY OF ANY PATENTS OR THE NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

ARTICLE 13
INDEMNIFICATION; INSURANCE

13.1 Indemnification of Bicycle. Genentech shall indemnify, defend and hold harmless BicycleTx, its Affiliates and its and their respective directors, officers, employees, and agents (the "**BicycleTx Indemnitees**") from and against any and all losses, damages, liabilities, penalties, settlements, costs, taxes (including penalties and interest) and expenses (including reasonable attorneys' fees and other expenses of litigation) (collectively, "**Losses**") in connection with any and all suits, investigations, claims, or demands of Third Parties (collectively, "**Third Party Claims**") incurred by or rendered against the BicycleTx Indemnitees arising from or occurring as a result of: (a) the breach by Genentech or its Affiliates of this Agreement; (b) the negligence, recklessness or willful misconduct on the part of Genentech or its Affiliates or their respective directors, officers, employees, and agents in performing its or their obligations under this Agreement; or (c) the Exploitation of any Discovery Constructs or Licensed Products by Genentech or its Affiliates or Sublicensees; except, in the case of clauses (a) through (c) above, to the extent BicycleTx has an obligation to indemnify Genentech pursuant to Section 13.2.

13.2 Indemnification of Genentech. BicycleTx shall indemnify, defend and hold harmless Genentech, its Affiliates and its and their respective directors, officers, employees, and agents (the "**Genentech Indemnitees**") from and against any and all Losses in connection with any and all Third Party Claims incurred by or rendered against the Genentech Indemnitees arising from or occurring as a result of: (a) the breach by BicycleTx or its Affiliates of this Agreement; (b) the negligence, recklessness or willful misconduct on the part of BicycleTx or its Affiliates or its or their respective directors, officers, employees, and agents in performing its obligations under this Agreement; or (c) the Exploitation of any Discovery Constructs by BicycleTx or its Affiliates pursuant to the practice of any Unblocking License following termination of this Agreement; except, in the case of clauses (a) through (c) above, to the extent Genentech has an obligation to indemnify BicycleTx pursuant to Section 13.1.

13.3 Notice of Claim. All indemnification claims in respect of a Party, its Affiliates, or its or their respective directors, officers, employees and agents shall be made solely by such Party to this Agreement (the "**Indemnified Party**"). The Indemnified Party shall give the indemnifying Party (the "**Indemnifying Party**") prompt written notice (an "**Indemnification Claim Notice**") of any Losses or

discovery of fact upon which such Indemnified Party intends to base a request for indemnification under this ARTICLE 13, but in no event shall the Indemnifying Party be liable for any Losses that result from any delay by the Indemnified Party in providing such notice. Each Indemnification Claim Notice must contain a description of the claim and the nature and amount of such Loss (to the extent that the nature and amount of such Loss is known at such time). The Indemnified Party shall furnish promptly to the Indemnitee copies of all papers and official documents received in respect of any Losses and Third Party Claims.

13.4 Control of Defense. The Indemnifying Party shall have the right, but not the obligation, to conduct and control, through counsel of its choosing, any action for which indemnification is sought, and if the Indemnifying Party elects to assume the defense thereof, the Indemnifying Party shall not be liable to the Indemnified Party for any legal expenses of other legal counsel or any other expenses subsequently incurred by such Indemnified Party in connection with the defense thereof. The Indemnifying Party may settle any action, claim or suit for which the Indemnified Party is seeking indemnification; provided that the Indemnifying Party shall first give the Indemnified Party advance written notice of any proposed compromise or settlement and such Indemnified Party provides prior written approval, such approval not to be unreasonably withheld or delayed. The Parties and their employees shall cooperate fully with each other and their legal representatives in the investigation, defense, prosecution, negotiation, or settlement of any such claim or suit. Each Party's indemnification obligations under this ARTICLE 13 shall not apply to amounts paid by an Indemnified Party in settlement of any action with respect to a Third Party claim, if such settlement is effected without the prior written consent of the Indemnifying Party, which consent shall not be withheld unreasonably. In no event shall the Indemnifying Party settle or abate any Third Party Claim in a manner that would diminish the rights or interests of the Indemnified Party, admit any liability, fault or guilt by the Indemnified Party or obligate the Indemnified Party to make any payment, take any action, or refrain from taking any action, without the prior written approval of the Indemnified Party.

13.5 Limitation of Liability. EXCEPT FOR DAMAGES PAYABLE FOR A PARTY'S BREACH OF ITS OBLIGATIONS UNDER ARTICLE 11 (BASED ON REASONABLE WRITTEN EVIDENCE) OR REQUIRED TO BE PAID PURSUANT TO A PARTY'S INDEMNIFICATION OBLIGATIONS UNDER THIS ARTICLE 13, NEITHER PARTY NOR ANY OF ITS AFFILIATES SHALL BE LIABLE FOR INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE OR CONSEQUENTIAL DAMAGES, INCLUDING LOSS OF PROFITS OR BUSINESS INTERRUPTION, HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER IN CONTRACT, TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY OR OTHERWISE IN CONNECTION WITH THIS AGREEMENT OR THE EXERCISE OF ANY LICENSE GRANTED HERUNDER, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

13.6 Insurance. Each Party shall obtain and carry in full force and effect the minimum insurance requirements set forth herein. Such insurance (a) shall be primary insurance with respect to each Party's own participation under this Agreement, (b) shall be issued by a recognized insurer [***], (c) shall list the other Party as an additional named insured thereunder, and (d) shall require [***] written notice to be given to the other Party prior to any cancellation, non-renewal or material change thereof.

13.6.1 Types and Minimum Limits. The types of insurance, and minimum limits shall be:

(a) [***].

(b) [***].

(c) [***].

13.6.2 Certificates of Insurance. Upon request by a Party, the other Party shall provide Certificates of Insurance evidencing compliance with this Section 13.6 (including evidence of permitted self-insurance, as applicable). The insurance policies shall be under an occurrence form, but if only a claims-made form is available to a Party, then such Party shall continue to maintain such insurance after the expiration or termination of this Agreement for the longer of (a) a period of [***] following termination or expiration of this Agreement in its entirety, or (b) with respect to a particular Party, last sale of a Licensed Product (or but for expiration or termination, would be considered a Licensed Product) sold under this Agreement by a Party.

13.6.3 Self-Insurance. Notwithstanding the foregoing in this Section 13.6, a Party may self-insure, in whole or in part, the insurance requirements described above, provided that such Party (on a consolidated basis with its Affiliates) [***], provides, upon request of the other Party, reasonable evidence thereof to such other Party.

ARTICLE 14
TERM AND TERMINATION

14.1 Term. This Agreement shall commence on the Effective Date and, unless earlier terminated in accordance herewith, shall continue in force and effect on a Collaboration Program-by-Collaboration Program basis, until the later of (a) the completion or termination of all Discovery Research Activities for such Collaboration Program without Genentech delivering a Dev Go Notice for any Collaboration Program, or (b) if Genentech delivers a Dev Go Notice for such Collaboration Program, the expiration of the Royalty Term for all Licensed Products for such Collaboration Program in the Territory (such period, the "**Term**"); provided that, following the expiration of the Term under clause (b), on a Collaboration Program-by-Collaboration Program and country-by-country basis, the license grant to Genentech in Section 7.1 shall become non-exclusive, fully-paid, royalty-free and irrevocable.

14.2 Termination For Convenience. Genentech may terminate this Agreement in its entirety or on a Collaboration Program-by-Collaboration Program basis and/or Major Market-by-Major Market basis, for any or no reason, upon:

14.2.1 [***] prior written notice to BicycleTx if termination occurs prior to [***];

14.2.2 [***] prior written notice to BicycleTx if termination occurs after [***]; and

14.2.3 [***] days prior written notice to BicycleTx if termination occurs after [***].

With regard to termination of the Agreement in its entirety pursuant to this Section 14.2, the notice period shall be the period set forth in Section 14.2.1, Section 14.2.2 or Section 14.2.3 that is applicable to the Collaboration Program that is furthest advanced at the time of such termination.

If Genentech terminates this Agreement pursuant to this Section 14.2, Genentech shall grant, and hereby grants to BicycleTx and its Affiliates, as applicable, an Unblocking License for the applicable Terminated Target(s), and Section 14.6 shall apply.

14.3 Termination for Uncured Material Breach.

14.3.1 Material Breach. If either Party (the "**Non-Breaching Party**") believes that the other Party (the "**Breaching Party**") has materially breached one (1) or more of its material obligations under this Agreement, then the Non-Breaching Party may deliver notice of such material breach to the Breaching Party (a "**Breach Notice**"). If (a) the Breaching Party does not dispute that it has committed a material breach of one (1) or more of its material obligations under this Agreement, and (b) either (i) the Breaching Party fails to cure such breach within [***] after receipt of the Breach Notice ("**Breach Cure Period**"), or (ii) a cure cannot be fully achieved within such Breach Cure Period and the Breaching Party has failed to commence to cure or has failed to use diligent efforts to achieve a full cure within the Breach Cure Period or as soon thereafter as is reasonably possible, then the Non-Breaching Party may terminate this Agreement in whole or in part upon written notice to the Breaching Party, effective upon receipt by the Breaching Party. If the Breaching Party disputes in good faith that it has materially breached one (1) or more of its material obligations under this Agreement or that it has failed to timely or diligently cure such material breach, the Dispute shall be resolved pursuant to Section 15.7 and the Breach Cure Period shall be tolled until such dispute is so resolved. Upon a determination of material breach or failure to cure, the Breaching Party may have the remainder of the Breach Cure Period to cure such material breach. If such material breach is not cured within the Breach Cure Period, then absent withdrawal of the Non-Breaching Party's request for termination, this Agreement shall terminate in whole or in part (i.e., for the Terminated Target or the Terminated Asset(s) in the applicable Terminated Territories), effective as of the expiration of the Breach Cure Period.

14.3.2 Adverse Ruling. Furthermore, if as a result of the application Section 15.7, the Breaching Party is determined to be in material breach of one (1) or more of its material obligations under this Agreement, such that the Non-Breaching Party has the right to terminate this Agreement in whole (or in part under Section 14.3.3 or 14.3.4) (an "**Adverse Ruling**") and the Breaching Party fails to complete the actions specified in such Adverse Ruling, or to cure such material breach within [***] after such Adverse Ruling, or such other period (which may be shorter) as the Arbitrator may provide in such Adverse Ruling, then the Non-Breaching Party may terminate this Agreement in whole or in part upon written notice to the Breaching Party.

14.3.3 Genentech's Uncured Material Breach of Diligence Obligations Following Dev Go. Notwithstanding Section 14.3.1, if the material breach and failure to cure contemplated by Section 14.3.1 is with respect to Genentech's Development or Commercialization diligence obligations under Section 5.1 or Section 6.2 respectively solely with respect to [***]

[***]. For clarity, termination under this Section 14.3.3 may occur only on a Collaboration Program-by-Collaboration Program basis.

14.3.4 Genentech's Uncured Material Breach prior to Dev Go. Notwithstanding Section 14.3.1, if the material breach and failure to cure contemplated by Section 14.3.1 is solely with respect to Genentech's obligations under this Agreement with respect to any single Collaboration Program prior to Dev Go, BicycleTx shall not have the right to terminate this Agreement in its entirety, but shall have the right to terminate this Agreement solely with respect to such Collaboration Program. For clarity, a termination of a single Collaboration Program under this Section 14.3.4 shall not affect the rights and obligations of the Parties with regard to the use of Targeting Arms that were the subject of activities in the terminated Collaboration Program, to the extent such Targeting Arms are the subject of activities in other then-ongoing Collaboration Programs or activities outside this Agreement as permitted under this Agreement.

14.4 Termination for Insolvency. If either Party (a) files for protection under bankruptcy or insolvency laws, (b) makes an assignment for the benefit of creditors, (c) appoints or suffers appointment of a receiver or trustee over substantially all of its property that is not discharged within ninety (90) days after such filing, (d) is a party to any dissolution or liquidation, (e) files a petition under any bankruptcy or insolvency act or has any such petition filed against it that is not discharged within ninety (90) days of the filing thereof, or (f) admits in writing its inability generally to meet its obligations as they fall due in the general course, then the other Party may terminate this Agreement in its entirety effective immediately upon written notice to such Party.

14.5 Rights in Bankruptcy.

14.5.1 Applicability of 11 U.S.C. § 365(n). All rights and licenses (collectively, the "**Intellectual Property**") granted under or pursuant to this Agreement, including all rights and licenses to use improvements or enhancements developed during the Term, are intended to be, and shall otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code (the "**Bankruptcy Code**") or any analogous provisions in any other country or jurisdiction, licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code. The Parties agree that the licensee of such Intellectual Property under this Agreement shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code, including Section 365(n) of the Bankruptcy Code, or any analogous provisions in any other country or jurisdiction. All of the rights granted to either Party under this Agreement shall be deemed to exist immediately before the occurrence of any bankruptcy case in which the other Party is the debtor.

14.5.2 Rights of non-Debtor Party in Bankruptcy. If a bankruptcy proceeding is commenced by or against either Party under the Bankruptcy Code or any analogous provisions in any other country or jurisdiction, the non-debtor Party shall be entitled to a complete duplicate of (or complete access to, as appropriate) any Intellectual Property and all embodiments of such Intellectual Property, which, if not already in the non-debtor Party's possession, shall be delivered to the non-debtor Party within [***] of such request; provided, that the debtor Party is excused from its obligation to deliver the

Intellectual Property to the extent the debtor Party continues to perform all of its obligations under this Agreement and the Agreement has not been rejected pursuant to the Bankruptcy Code or any analogous provision in any other country or jurisdiction.

14.6 Effects of Termination.

14.6.1 Termination by Genentech for Convenience or by BicycleTx for Genentech's Uncured Material Breach or Genentech's Insolvency. In the event of a termination of this Agreement in its entirety or in part by Genentech pursuant to Section 14.2 or by BicycleTx pursuant to Section 14.3 or 14.4, then the following terms of this Section 14.6.1 shall apply:

(a) Subject to Section 14.6.1(d), the rights and licenses granted by BicycleTx to Genentech under this Agreement shall terminate with regard to all applicable Terminated Targets, Terminated Assets and/or Terminated Territories, as of the effective date of termination. If such termination occurs [***], then, if [***] the applicable Terminated Assets or Terminated Targets [***], the Parties shall [***] with regard to the applicable Terminated Targets and Terminated Assets.

(b) In the case of termination after Dev Go for a given Collaboration Program, Genentech shall, within [***] following the effective date of termination (or in the case of termination by Genentech for convenience, no later than the effective date of termination) ("**Initial Reversion Package Period**"), provide copies to BicycleTx, [***], of (i) a summary of [***] and (ii) a good faith estimate of [***] then available to Genentech (the "**Initial Reversion Package**"). Within [***] following the delivery of the Initial Reversion Package, BicycleTx shall notify Genentech in writing whether it wishes to conduct or not to conduct more extensive diligence in order to evaluate the BicycleTx Option pursuant to Section 14.6.1(c). If BicycleTx provides timely notice for more extensive diligence, then the Parties shall discuss in good faith and agree what additional information relating to the applicable Terminated Assets would be [***] for BicycleTx to assess whether to exercise the BicycleTx Option (as defined below) and reasonably assess the value of the program for the purposes of negotiating Reversion Terms (as defined below), taking into consideration what additional information Genentech can reasonably provide, while [***], to facilitate BicycleTx's evaluation (the "**Secondary Reversion Package**", and together with the Initial reversion Package, the "**Reversion Packages**"). Any such discussion and transfer of the Secondary Reversion Package shall be completed within [***] of BicycleTx's notice to Genentech under this Section 14.6.1(b) ("**Secondary Reversion Package Period**"). The Parties shall agree upon a procedure for BicycleTx to evaluate [***]. BicycleTx shall have the right to use the Reversion Packages solely to evaluate whether to exercise the BicycleTx Option below, and for no other purpose.

(c) Commencing upon the date of termination and ending [***] following delivery of the last of the Reversion Packages from Genentech to BicycleTx (the "**Option Period**"),

BicycleTx will have an option (the "**BicycleTx Option**") to obtain from Genentech (i) a worldwide, royalty-bearing, sublicensable (through multiple tiers) license to Exploit the applicable Terminated Asset(s) in the applicable Territory(ies) under (A) Patents and Know How Controlled by Genentech ([***]) that are [***] to Exploit the applicable Terminated Assets, (B) to the extent not assigned to BicycleTx under the following subclause (ii), Genentech's interest in Joint Collaboration Patents and Joint Collaboration Know-How, and (C) any Product Trademarks Controlled by Genentech, and (ii) an assignment of Genentech's interest in Joint Collaboration Patents and Joint Collaboration Know-How that (1) was [***] for the Collaboration Program including such Terminated Assets, and (2) [***] the Exploitation of the Terminated Assets in the applicable Territories [***], provided that for clarity, no assignment shall be required with respect to Genentech's interest in Joint Collaboration Patents and Joint Collaboration Know-How [***] for the applicable Collaboration Program (collectively the rights, license and intellectual property in (i) and (ii), the "**Reversion Rights**"). In the event of the foregoing assignment by Genentech of its interest in Joint Collaboration Patents and Joint Collaboration Know-How, BicycleTx [***]. If BicycleTx does not exercise the BicycleTx Option, then [***]. If BicycleTx exercises the BicycleTx Option, then the Parties shall [***] with regard to the applicable Terminated Targets and Terminated Assets.

(d) The Parties will negotiate commercially reasonable terms, taking into account the then current stage of the applicable Terminated Assets in the applicable Terminated Territories ("**Reversion Terms**"), which shall be negotiated in good faith by the Parties within [***] following the exercise of the BicycleTx Option by BicycleTx ("**Negotiation Period**") and contained in a written reversion agreement to be concluded and executed by and between the Parties ("**Reversion Agreement**").

(e) If the Parties are unable to agree on the Reversion Terms of a Reversion Agreement within the Negotiation Period, such Dispute shall be submitted for final resolution binding arbitration pursuant to Section 14.6.2.

[***]

[***]

[***]

14.6.3 Termination by Genentech for BicycleTx's Uncured Material Breach or Insolvency. In the event of a termination by Genentech pursuant to Section 14.3 for BicycleTx's uncured material breach or Section 14.4 for BicycleTx's insolvency, all rights and licenses granted by one Party to the other Party under this Agreement shall terminate on the effective date of termination, (i) prior to Dev Go, in their entirety or with respect to each Terminated Target, and (ii) after Dev Go with respect to Terminated Assets in the applicable Terminated Territories, as applicable. In addition, the following terms shall apply:

(a) BicycleTx will have no further obligations under this Agreement with respect to the Terminated Targets or Terminated Assets, including any obligations under ARTICLE 5, other than, for clarity, any damages resulting from BicycleTx's breach that Genentech may be awarded in connection with any final resolution of a Dispute under Section 15.7, regardless of whether Genentech has terminated the Agreement in its entirety or in part with regard to the applicable Terminated Target or Terminated Asset, [***].

(b) Genentech will have no further obligations under this Agreement with respect to Terminated Targets or Terminated Assets in the applicable Terminated Territories, including any obligations under ARTICLE 8.

14.7 Rights in Lieu of Termination. Following the delivery of an Dev Go Notice for a given Collaboration Program, if Genentech has the right to terminate this Agreement in its entirety or with respect to a given Collaboration Program pursuant to Section 14.3 (i.e. by mutual agreement of the Parties regarding a material breach by BicycleTx or as may be finally determined in an Adverse Ruling following final resolution under Section 15.7), then within [***] following the expiration of the relevant cure period, if any, Genentech may, by written notice to BicycleTx, and as its sole and exclusive remedy in lieu of exercising its right under Section 14.3 with respect to such breach, and in lieu of any other remedy, elect to continue this Agreement (in its entirety or with respect to the affected Collaboration Program) as modified by this Section 14.7, in which case, effective as of the date Genentech delivers notice of such election to BicycleTx:

14.7.1 all rights and licenses granted by Genentech under the Agreement to BicycleTx shall immediately terminate with respect to all affected Collaboration Programs;

14.7.2 all rights and licenses granted by BicycleTx shall survive;

14.7.3 BicycleTx's obligations under this Agreement will remain in force, provided that BicycleTx will have no further obligations under this Agreement with respect to the performance of Discovery Research Activities or in connection with Development Candidates or Licensed Products relating to the affected Collaboration Programs;

14.7.4 BicycleTx will continue to perform its obligations with respect to BicycleTx Background Patents and BicycleTx Program Patents pursuant to Section 9.4; and

14.7.5 all provisions of this Agreement with respect to Genentech's rights and obligations shall apply, provided that, without limiting Section 13.5, and in lieu of damages to which Genentech may otherwise have been entitled as a result of the Adverse Ruling as a consequence of BicycleTx's material breach, the Parties will require that the arbitrator include in any Adverse Ruling following final resolution under Section 15.7, or in the absence of such an arbitration proceeding, the Parties [***] payable by Genentech to BicycleTx in connection with Development Candidates and Licensed Products included in the affected Collaboration Programs, taking into consideration: [***], provided that if, despite good faith discussions, the Parties are unable to agree on the equitable reduction, then the Dispute regarding the appropriate reduction, if any, shall be resolved pursuant to Section 15.7.

14.8 Termination of Terminated Territory. In the event of a termination of this Agreement with respect to a Terminated Territory (but not in the case of any termination of this Agreement in its entirety), the term "Territory" shall be automatically amended to exclude the Terminated Territory and all rights and licenses granted by BicycleTx hereunder (a) shall automatically be deemed to be amended to exclude, if applicable, the right to market, promote, detail, distribute, import, sell, offer for sale, file any Drug Approval Application for, or seek any Regulatory Approval for Compounds or Licensed Products in such Terminated Territory, and (b) shall otherwise survive and continue in effect in such Terminated Territory solely for the purpose of furthering any Commercialization of the Compounds or Licensed Products in the Territory other than the Terminated Territory or any Development or Manufacturing in support thereof.

14.9 Accrued Rights; Surviving Obligations.

14.9.1 Termination or expiration of this Agreement (either in its entirety or with respect to one (1) or more Terminated Territories or with respect to a Terminated Target or Terminated Asset) for any reason shall be without prejudice to any rights that shall have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration shall not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement. Without limiting the foregoing, the following Articles and Sections of this Agreement shall survive the termination or expiration of this Agreement for any reason: Articles 1 (Definitions), 11 (Confidentiality and Non-Disclosure; excluding Section 11.5 [***]), 13 (Indemnification; Insurance), and 15 (Miscellaneous), and Sections 2.3.2(e)-2.3.2(i) (Antigen Targets; Targeting Arms), 2.5.1(e) (LSR Go), 2.5.3 (Termination of Discovery Research Activities for a Collaboration Program), 3.2.7 (Effects of Target Substitution), 5.3 (Transfer of CMC Materials prior to Dev Go), 5.6.3 (Records), 7.3 (Mutual Grants), 7.6 (Retention of Rights), 7.7 (No Implied Licenses), 8.14 (Audit), 8.15 (Audit Dispute), 8.16 (Confidentiality), 9.1 (Ownership of Intellectual Property), 9.3 (Assignment Obligation), 9.4.4 (Genentech Collaboration Patents and Joint Collaboration Patents; solely with respect to Joint Collaboration Patents); 9.11 (Common Interest), 14.1 (Term), 14.2 (Termination for Convenience), 14.5 (Rights in Bankruptcy), 14.6 (Effects of Termination), 14.8 (Termination of Terminated Territory), and 14.9 (Accrued Rights; Surviving Obligations). If this Agreement is terminated with respect to a Terminated Territory or

a Terminated Target but not in its entirety, then following such termination the foregoing provisions of this Agreement shall remain in effect with respect to the Terminated Territory or Terminated Target, as applicable (to the extent they would survive and apply in the event the Agreement expires or is terminated in its entirety), and all provisions not surviving in accordance with the foregoing shall terminate upon termination of this Agreement with respect to the Terminated Territory, Terminated Target or Terminated Asset, as applicable and be of no further force and effect (and, for purposes of clarity, all provisions of this Agreement shall remain in effect with respect to all countries in the Territory other than the Terminated Territory or with respect to the Collaboration Target other than the Terminated Target).

14.9.2 Notwithstanding the termination of Genentech's licenses and other rights under this Agreement or with respect to a particular Major Market or country or other jurisdiction or with respect to a Terminated Target, as the case may be, if this Agreement is terminated in its entirety or in part by Genentech pursuant to Section 14.3 or 14.4, with BicycleTx's prior written consent, not to be unreasonably withheld, for up to [***] after the effective date of such termination with respect to each Major Market or country or other jurisdiction or Terminated Target with respect to which such termination applies, Genentech may continue to sell or otherwise dispose of all Licensed Product then in its inventory and any in-progress inventory, in each case that is intended for sale or disposition in such Major Market or country or other jurisdiction or, in the case of a Terminated Target, in the Territory, as though this Agreement had not terminated with respect to such Major Market or country or other jurisdiction or Terminated Target, as applicable, and such sale or disposition shall not constitute infringement of BicycleTx's or its Affiliates' Patent or other intellectual property or other proprietary rights. For purposes of clarity, Genentech shall continue to make payments thereon as provided in ARTICLE 8 (as if this Agreement had not terminated with respect to such Major Market or country or other jurisdiction or Terminated Target, as applicable).

ARTICLE 15
MISCELLANEOUS

15.1 Force Majeure. Neither Party shall be held liable or responsible to the other Party or be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from events beyond the reasonable control of the non-performing Party, including fires, floods, earthquakes, hurricanes, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts, or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), acts of God, or acts, omissions or delays in acting by any governmental authority (except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement). The non-performing Party shall notify the other Party of such force majeure within [***] after such occurrence by giving written notice to the other Party stating the nature of the event, its anticipated duration, and any action being taken to avoid or minimize its effect. The suspension of performance shall be of no greater scope and no longer duration than is necessary and the non-performing Party shall use commercially reasonable efforts to remedy its inability to perform.

15.2 Export Control. This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States or other countries that may be imposed on the Parties from time to time. Each Party agrees that it will not export, directly or indirectly, any technical information acquired from the other Party under this Agreement or any products using such technical information to a location or in a manner that at the time of export requires an export license or other

governmental approval, without first obtaining the written consent to do so from the appropriate agency or other governmental entity in accordance with Applicable Law.

15.3 Assignment. Neither Party shall sell, transfer, assign, delegate, pledge, or otherwise dispose of, whether voluntarily, involuntarily, by operation of law or otherwise, this Agreement or any of its rights or obligations hereunder without the prior written consent of the other Party, such consent not to be unreasonably withheld, conditioned or delayed; provided, that either Party may make such an assignment without the other Party's consent (a) to its Affiliate, provided that if the entity to which this Agreement is assigned ceases to be an Affiliate of the assigning Party, this Agreement will be automatically assigned back to the assigning Party or its successor or (b) to a successor, whether in a merger, sale of stock, sale of assets or any other transaction, of the business to which this Agreement relates. Any attempted assignment or delegation in violation of this Section 15.3 shall be void and of no effect. All validly assigned and delegated rights and obligations of the Parties hereunder shall be binding upon and inure to the benefit of and be enforceable by and against the successors and permitted assigns of BicycleTx or Genentech, as the case may be. The permitted assignee or transferee shall assume all obligations of its assignor or transferor under this Agreement. Without limiting the generality of the foregoing, the grant of rights set forth in this Agreement shall be binding upon any successor or permitted assignee of BicycleTx, and the obligations of Genentech (including all payment obligations), shall run in favor of any such successor or permitted assignee of BicycleTx's benefits under this Agreement. Notwithstanding the foregoing, all rights to Know-How, Patents, materials and other intellectual property Controlled by a Third Party permitted assignee of a Party (or any of such Third Party's affiliates immediately prior to the closing of such assignment) immediately prior to such assignment shall be automatically excluded from the rights licensed or granted to the other Party under this Agreement.

15.4 Effects of a Change of Control. If there is a Change of Control of BicycleTx, then BicycleTx shall provide written notice to Genentech at least [***] prior to the closing date of such Change of Control, subject to any confidentiality or other legal obligations of BicycleTx then in effect (but in any event Bicycle shall notify Genentech within [***] after the closing date of such Change of Control). Following the closing date of the Change of Control, the Change of Control Group in connection with such Change of Control shall Segregate any Segregation Products (if any).

15.5 Severability. If any provision of this Agreement is held to be illegal, invalid, or unenforceable under any present or future law, and if the rights or obligations of either Party under this Agreement will not be materially and adversely affected thereby, (a) such provision shall be fully severable, (b) this Agreement shall be construed and enforced as if such illegal, invalid, or unenforceable provision had never comprised a part hereof, (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid, or unenforceable provision or by its severance from this Agreement, and (d) in lieu of such illegal, invalid, or unenforceable provision, there shall be added automatically as a part of this Agreement a legal, valid, and enforceable provision as similar in terms to such illegal, invalid, or unenforceable provision as may be possible and reasonably acceptable to the Parties.

15.6 Governing Law, Jurisdiction and Service.

15.6.1 Governing Law. This Agreement or the performance, enforcement, breach or termination hereof shall be interpreted, governed by and construed in accordance with the laws of the State of New York, United States excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction; provided, that all questions concerning (a) inventorship of Patents under this Agreement shall be determined

in accordance with Section 9.2 and (b) the construction or effect of Patents shall be determined in accordance with the laws of the country or other jurisdiction in which the particular Patent has been filed or granted, as the case may be. The Parties agree to exclude the application to this Agreement of the United Nations Convention on Contracts for the International Sale of Goods.

15.6.2 Service. Each Party further agrees that service of any process, summons, notice or document by registered mail to its address set forth in Section 15.8.2 shall be effective service of process for any action, suit, or proceeding brought against it under this Agreement in any such court.

15.7 Dispute Resolution. Except as provided in Section 8.15, Section 14.6.2 and Section 15.7.2, any dispute arising out of or relating to this Agreement that has not been resolved at the JRC or otherwise under the terms of this Agreement, including the determination of the scope or applicability of this Section 15.7 and the agreement to arbitrate, or any document or instrument delivered in connection herewith (a "**Dispute**"), it shall be resolved pursuant to this Section 15.7.

15.7.1 General. Any Dispute shall first be referred to the Alliance Managers who will seek to resolve the issue within [***]. If no resolution is obtained, the issue will be elevated to the Senior Officers of the Parties, who shall confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the Senior Officers shall be conclusive and binding on the Parties. If the Senior Officers are not able to agree on the resolution of any such issue within [***] (or such other period of time as mutually agreed by the Senior Officers) after such issue was first referred to them, then, except as otherwise set forth in Section 15.7.2, the Dispute shall be finally settled by arbitration as set forth in Section 15.7.3. Any dispute concerning the commencement of the arbitration shall be finally settled by the arbitrators.

15.7.2 Intellectual Property Disputes. If a Dispute arises with respect to the validity, scope, enforceability, inventorship or ownership of any Patent, Trademark or other intellectual property rights, and such Dispute cannot be resolved in accordance with Section 15.7.1, unless otherwise agreed by the Parties in writing, such Dispute shall not be submitted to an arbitration proceeding in accordance with Section 15.7.3 and instead, either Party may initiate litigation in a court of competent jurisdiction, notwithstanding Section 15.6, in any country or other jurisdiction in which such rights apply. This notwithstanding, the Parties expressly waive any right to a jury trial in connection with disputes under this Section 15.7.2. In case of a Dispute between the Parties with respect to inventorship, the Parties shall jointly select a patent attorney registered before the United States Patent and Trademark Office and submit such Dispute to the mutually-selected patent attorney for resolution by expert determination under the United States patent law. The decision of such patent attorney with respect to inventorship shall be final, and the Parties agree to be bound by the decision and share equally the expenses of such patent attorney. If, within [***] after the Senior Officers have failed to settle a Dispute regarding inventorship the Parties have not been able to mutually agree on the selection of a patent attorney for such expert determination, each Party shall appoint a patent counsel within [***] and both Party-appointed patent counsels shall, within [***] following the last appointment of a patent counsel by a Party, nominate the patent counsel who will conduct the expert determination under this Section 15.7.2.

15.7.3 Arbitration. Any arbitration shall take place in accordance with Schedule 15.7.3.

15.7.4 Adverse Ruling. Any determination pursuant to this Section 15.7 that a Party is in material breach of its material obligations hereunder shall specify a (nonexclusive) set of actions to be taken to cure such material breach, if feasible.

15.7.5 Interim Relief. Notwithstanding anything herein to the contrary in this Section 15.7, in the event that a Party reasonably requires relief on a more expedited basis than would be possible pursuant to the procedure set forth in this ARTICLE 15, such Party may seek interim or provisional relief, including a temporary restraining order, preliminary injunction or other interim equitable relief concerning a Dispute, if necessary to protect the interests of such Party. This Section 15.7.5 shall be specifically enforceable.

15.7.6 Pending Dispute. Good Faith Performance of Activities. During a pending Dispute, where this Agreement has not yet been terminated, each Party shall continue to perform in good faith its obligations under this Agreement.

15.8 Notices.

15.8.1 Notice Requirements. Any notice, request, demand, waiver, consent, approval, or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be deemed given only if (a) delivered by hand, (b) sent by facsimile transmission (with transmission confirmed), or (c) by internationally recognized overnight delivery service that maintains records of delivery, addressed to the Parties at their respective addresses specified in Section 15.8.2 or to such other address as the Party to whom notice is to be given may have provided to the other Party in accordance with this Section 15.8.1. Such notice shall be deemed to have been given as of the date delivered by hand or transmitted by facsimile (with transmission confirmed) or on the second Business Day (at the place of delivery) after deposit with an internationally recognized overnight delivery service. Any notice delivered by facsimile shall be confirmed by a hard copy delivered as soon as practicable thereafter. This Section 15.8.1 is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

15.8.2 Address for Notice.

If to Genentech, to:

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080
Attn: Corporate Secretary
Facsimile: [***]

with a copy (which shall not constitute notice) to:

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080
Attn: Pharma Partnering, Alliance Management
Facsimile: [***]

If to BicycleTx, to:

Bicycle Therapeutics Limited
Building 900
Babraham Research Campus
Cambridge, CB22 3AT
United Kingdom
Attention: Chief Operating Officer

with a copy (which shall not constitute notice) to:

Cooley LLP
3175 Hanover Street
Palo Alto, CA 94304
Attention: Laura Berezin
Facsimile: [***]

15.9 Entire Agreement; Amendments. This Agreement, together with the Schedules attached hereto, sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof and all prior agreements, understandings, promises, and representations, whether written or oral, with respect thereto are superseded hereby (including the Prior NDA). The foregoing shall not be interpreted as a waiver of any remedies available to either Party as a result of any breach by the other Party (or its Affiliates) of its obligations under the Prior NDA, prior to the Effective Date. Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth in this Agreement. No amendment, modification, release, or discharge with respect to this Agreement shall be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

15.10 English Language. This Agreement shall be written and executed in, and all other communications under or in connection with this Agreement shall be in, the English language. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

15.11 Waiver and Non-Exclusion of Remedies. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right hereunder or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

15.12 No Benefit to Third Parties. Except as provided in ARTICLE 13, covenants and agreements set forth in this Agreement are for the sole benefit of the Parties hereto and their successors and permitted assigns, and they shall not be construed as conferring any rights on any other Persons.

15.13 Further Assurance. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or

as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof, or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

15.14 Relationship of the Parties. It is expressly agreed that BicycleTx, on the one hand, and Genentech, on the other hand, shall be independent contractors and that the relationship between the Parties shall not constitute a partnership, joint venture, or agency including for all tax purposes. Neither BicycleTx nor Genentech shall have the authority to make any statements, representations, or commitments of any kind, or to take any action, which shall be binding on the other Party, without the prior written consent of the other Party to do so. All persons employed by a Party shall be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such Party. The Parties (and any successor, assignee, transferee, or Affiliate of a Party) shall (a) use commercially reasonable efforts to structure the arrangement and activities contemplated by this Agreement to avoid the arrangement contemplated by this Agreement being treated as a partnership that is engaged in a "United States trade or business" for United States tax purposes and (b) not treat or report the relationship between the Parties arising under this Agreement as a partnership for United States tax purposes, without the prior written consent of the other Party unless required by a final "determination" as defined in Section 1313 of the United States Internal Revenue Code of 1986, as amended.

15.15 Performance by Affiliates. Each Party may use one (1) or more of its Affiliates to perform its obligations and duties hereunder and such Affiliates are expressly granted certain rights herein to perform such obligations and duties; provided that each such Affiliate shall be bound by the corresponding obligations of such Party; and provided further that the assigning Party, subject to an assignment to such Affiliate pursuant to Section 15.3, shall remain liable hereunder for the prompt payment and performance of its obligations hereunder.

15.16 Counterparts; Facsimile Execution. This Agreement may be executed in two (2) counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Agreement may be executed by facsimile or electronically transmitted signatures and such signatures shall be deemed to bind each Party hereto as if they were original signatures.

15.17 References. Unless otherwise specified, (a) references in this Agreement to any Article, Section or Schedule shall mean references to such Article, Section or Schedule of this Agreement, (b) references in any Section to any clause are references to such clause of such Section, and (c) references to any agreement, instrument, or other document in this Agreement refer to such agreement, instrument, or other document as originally executed or, if subsequently amended, replaced, or supplemented from time to time, as so amended, replaced, or supplemented and in effect at the relevant time of reference thereto.

15.18 Schedules. In the event of any inconsistencies between this Agreement and any schedules or other attachments hereto, the terms of this Agreement shall control.

15.19 Construction. Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders and the word "or" is used in the inclusive sense (and/or) unless the subjects of the conjunction are, or are intended to be, mutually exclusive. Whenever this Agreement refers to a number of days, unless otherwise specified, such number refers to calendar days. The captions of this Agreement are for convenience of reference only and in no way define, describe, extend, or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The term "including," "include," or "includes" as used

herein shall mean "including, but not limited to," and shall not limit the generality of any description preceding such term. The language of this Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party hereto. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provisions.

[*SIGNATURE PAGE FOLLOWS***]**

THIS DISCOVERY COLLABORATION AND LICENSE AGREEMENT is executed by the authorized representatives of the Parties as of the Effective Date.

BICYCLETX LIMITED	**GENENTECH, INC.**
By: /s/ Kevin Lee	By: /s/ Edward Harrington
Name: Dr. Kevin Lee	Name: Edward Harrington
Title: CEO	Title: CFO, Genentech

Schedule 1.60

Dev Go Criteria for the Initial Collaboration Targets

[***]

Schedule 1.66

Discovery Construct Threshold

[***]

Schedule 1.69

Initial Discovery Research Plan

[***]

Schedule 1.81

Existing Targeting Arms

[***]

Schedule 1.111

Genentech Reserved Targets

[***]

Schedule 1.113

Genentech Specified Countries

[***]

Schedule 1.120

Hit Success Criteria for the Initial Collaboration Targets

[***]

Schedule 1.128

Initial Collaboration Targets

[***]

Schedule 1.150

LSR Go Criteria for the Initial Collaboration Targets

[***]

Schedule 2.3.2

Part 1 - Genentech Targeting Arms of Interest

- [***]

Part 2 – [***] Terms of the [***] License

[***]

Part 3 – Targeting Arm Criteria applicable to the [***] **Targeting Arm**

- [***]

Schedule 12.2.1

Existing Patents

[***]

Schedule 15.7.3

Arbitration

1. **Rules**. Except as otherwise expressly provided in the Agreement (including under Section 15.7.2 of the Agreement), any Dispute that is not resolved amicably pursuant to Section 15.7 of the Agreement shall be referred to and finally resolved through arbitration administered by JAMS pursuant to its International Arbitration Rules and Procedures (the "**Rules**"), except as modified herein.

2. **Arbitrators; Seat**. The arbitral tribunal shall be comprised of three arbitrators. Each Party shall select one (1) arbitrator, and the two (2) arbitrators so selected shall choose a third arbitrator, who shall serve as president of the tribunal, within [***] of the second arbitrator's appointment. All three (3) arbitrators shall serve as neutrals, be impartial and independent, and have at least [***]. If a Party fails to nominate its arbitrator, or if the Parties' arbitrators cannot agree on the third, the necessary appointments shall be made in accordance with the Rules. The seat, or legal place, of arbitration shall be New York, New York, USA. The arbitration proceedings and all pleadings and written evidence shall be in the English language. Any written evidence originally in another language shall be submitted in English translation accompanied by the original or a true copy thereof.

3. **Procedures; Awards**. Each Party agrees to use reasonable efforts to make all of its current employees available, if reasonably needed, and agrees that the arbitrators may determine any person as necessary. The arbitrators shall be instructed to render a written, binding, non-appealable resolution and award on each issue that clearly states the basis upon which such resolution and award is made. The written resolution and award shall be delivered to the Parties as expeditiously as possible, but in no event more than [***] after conclusion of the hearing or the final written submissions, whichever is later, unless otherwise agreed by the Parties or determined by the arbitrators. The award shall be final and binding and the Parties undertake to carry out the award without delay. Judgment upon such award may be entered in any competent court. Each Party agrees that, notwithstanding any provision of applicable law or of this Agreement, it will not request, and the arbitrators shall have no authority to award, punitive or exemplary damages against any Party.

4. **Costs**. The prevailing Party, as determined by the arbitrators, shall be entitled to: (a) its share of fees and expenses of the arbitrators; and (b) its reasonable attorneys' fees and associated costs and expenses. In determining which Party "prevailed," the arbitrators shall consider: [***]. If the arbitrators determine that, given the scope of the arbitration, neither Party "prevailed," the arbitrators shall order that the Parties: (A) share equally the fees and expenses of the arbitrators; and (B) bear their own attorneys' fees and associated costs and expenses.

5. **Interim Equitable Relief.** Notwithstanding anything to the contrary in this Schedule 15.7.3, either Party may seek a temporary injunction or other interim equitable relief in a court of competent jurisdiction pending the ability of the arbitrators to review the decision under this Schedule 15.7.3. Such court shall have no jurisdiction or ability to resolve Disputes beyond the specific issue of temporary injunction or other interim equitable relief.

6. **Protective Orders; Arbitrability**. At the request of either Party, the arbitrators shall enter an appropriate protective order to maintain the confidentiality of information produced or exchanged in the course of the arbitration proceedings. The arbitrators shall have the power to decide all questions of

arbitrability. Except for purposes of confirming or enforcing an award, court proceedings to obtain interim relief, or as may be required by law, the existence of the Dispute, any settlement negotiations, the arbitration, any submissions (including exhibits, testimony, proposed rulings, and briefs), any rulings and the award shall be deemed to be Confidential Information of both Parties. The arbitrators shall have the authority to impose sanctions for unauthorized disclosure of Confidential Information.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-231718) of Bicycle Therapeutics plc of our report dated March 10, 2020 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Cambridge, United Kingdom
March 10, 2020

Exhibit 31.1

CERTIFICATION

I, Kevin Lee, certify that:

1. I have reviewed this Annual Report on Form 10-K of Bicycle Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2020

By: /s/ Kevin Lee
Kevin Lee, Ph.D., MBA
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Lee Kalowski, certify that:

1. I have reviewed this Annual Report on Form 10-K of Bicycle Therapeutics plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2020

By: /s/ Lee Kalowski
Lee Kalowski, MBA
Chief Financial Officer and President

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Kevin Lee, Chief Executive Officer of Bicycle Therapeutics plc (the "Company"), and Lee Kalowski, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 10, 2020

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 10th day of March, 2020.

/s/ Kevin Lee	/s/ Lee Kalowski
Kevin Lee, Ph.D., MBA	Lee Kalowski, MBA
Chief Executive Officer	Chief Financial Officer

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Bicycle Therapeutics plc under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.