Bicycle®

2025 | Annual Report

Bicycle®

April 2026

To Our Shareholders,

Bicycle Therapeutics made important progress in 2025 as our team focused on clinical execution to provide further validation of the Bicycle® technology platform. With recent regulatory guidance and a strategic reprioritization to focus on nuzefatide pevedotin (formerly BT5528) and next generation Bicycle® conjugates, including Bicycle® Radioconjugates (BRC®), we believe we are well positioned to make meaningful progress on our promising pipeline of next-generation therapeutics in our relentless pursuit of our mission to help patients live longer and live well.

The Bicycle® Advantage Has Potential to Lead to Enhanced Patient Benefits

Using our Bicycle technology, we are continuing our work to create medicines that can potentially deliver any payload to any target. Our Bicycle® molecules are designed to be highly selective and have minimal systemic exposure and off-target activity, which we believe will lead to longer, deeper and broader responses and potentially enhanced patient benefit. We call this The Bicycle Advantage.

The Bicycle Advantage continues to be demonstrated in clinical trial data from multiple clinical programs. We believe the unique features of Bicycle molecules have optimal properties for precision guided therapeutics in oncology as well as radiopharmaceuticals.

Drugging the Undruggable with Nuzefatide Pevedotin (BT5528)

Historically, multiple approaches to targeting Ephrin-A2 (EphA2) have been unsuccessful. Nuzefatide pevedotin, an EphA2 targeting Bicycle® Drug Conjugate (BDC®), creates a first-in-class opportunity for us to drug the undruggable and overcome the industry's historical safety and efficient delivery challenges. Results to date have shown nuzefatide pevedotin to demonstrate an emerging differentiated safety profile and encouraging preliminary anti-tumor activity in advanced solid tumors.

As we assess the relationship between EphA2 expression and activity, we believe we will benefit from additional research in an effort to validate a clear potential path forward in tumors where EphA2 is expressed. We look forward to evaluating important insights in the Phase 1/2 data being generated from nuzefatide pevedotin in combination with nivolumab and progressing our Phase 2 trial of nuzefatide pevedotin in adult patients with recurrent pancreatic ductal adenocarcinoma (PDAC).

Advancing Next-Generation Bicycle® Imaging Agents and Bicycle® Radioconjugates

Our strategy in radiopharmaceuticals is to utilize the versatility and modularity of our Bicycle technology to pursue novel targets with first-in-class potential by using isotopes that are best suited for each target. We believe Bicycle radioligand molecules are optimal for enhanced radioisotope delivery, showing high selectivity and tumor penetration with minimal systemic exposure in preclinical studies. As additional data are generated, we aim to further highlight how the advantages from Bicycle molecules delivering cytotoxic payloads also apply to delivering radioisotopes.

In 2025, additional human imaging data of a Bicycle® Imaging Agent (BIA) targeting MT1-MMP, our first radiopharmaceutical target, was presented which further highlighted the potential of MT1-MMP as a novel target in the treatment of cancer and demonstrated the positive properties of BIA molecules for radiopharmaceutical imaging. In addition, we presented preclinical data of an early BRC molecule targeting MT1-MMP, demonstrating the potential of Bicycle radioligands for theranostic use.

A BIA molecule moved into human imaging for EphA2 in 2025, our second radiopharmaceutical target, and we are excited to continue to progress our emerging radioligands pipeline this year. We look forward to building on this momentum and, having recently reported additional EphA2 human imaging data, now plan to initiate our first company-sponsored radioligand clinical trial for BT1702, an MT1-MMP targeting BRC carrying a ^{212}Pb radioisotope payload for theranostic use, in 2027.

End-to-End Supply Chain Supporting Radiopharmaceuticals Pipeline

Our progress in 2025 gives us the potential to advance a differentiated and isotope-agnostic radioligands pipeline. A bespoke set of agreements entered into in 2025 are designed to support the potential discovery, development and commercial supply of a portfolio of BRCs containing ^{212}Pb, building on the supply chains being established for a range of radioisotopes with Eckert & Ziegler. This provides us with a unique radiopharmaceutical capability from the identification of Bicycle targeting agents to the potential commercial supply of radiotherapeutics across multiple radioisotopes.

This end-to-end supply chain is anchored by a 15-year contract with the UK Nuclear Decommissioning Authority for access to up to 400 tonnes of continually regenerating reprocessed uranium (RepU). RepU continually regenerates providing a potentially sustainable supply of lead-212 (^{212}Pb), a radioisotope and one of the more potent therapeutic payloads against cancer cells known as Targeted Alpha Therapy. Pursuant to a collaboration with United Kingdom National Nuclear Laboratory, thorium-228 (^{228}Th) will be extracted and further processed into radium-224 (^{224}Ra), and loaded into ^{212}Pb generators, developed exclusively for Bicycle Therapeutics by SpectronRx, with initial quantities of ^{212}Pb successfully produced.

Zelenectide Pevedotin

In early 2026, we announced the successful completion of the dose selection portion of our Duravelo-2 trial in metastatic urothelial cancer, receiving regulatory alignment that the 6mg dose and schedule is optimal based on strong anti-tumor activity and its differentiated safety profile. However, based on the regulatory feedback we have received, the existing Duravelo-2 trial design is no longer considered acceptable as an approval path for zelenectide in metastatic urothelial cancer. Accordingly, we made the difficult decision to deprioritize this program for internal development and initiated a process to convert the Duravelo-2 trial to a randomized Phase 2 study.

In our view, these data further validate the ability of our Bicycle technology to deliver oncology therapeutics with a potentially improved benefit/risk profile compared to existing modalities. While we are disappointed for patients, we believe the strength of our data and clear medical need justify the continued development of zelenectide and look forward to determining the most appropriate path forward once more fulsome Duravelo-2 data is in hand.

The Future We Are Building

As our focus shifts towards progression of our next-generation pipeline, we feel we are well-positioned to leverage our resources to advance our promising technology and potentially provide next-generation therapeutics.

We are greatly appreciative of the patients and physicians who participate in our clinical trials, our partners, and our shareholders. I am also deeply grateful of our team and their disciplined execution and unwavering commitment to our mission to help patients live longer and live well.

Sincerely,

Kevin Lee, Ph.D.
Chief Executive Officer

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, 2025

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.)
Blocks A & B, Portway Building, Granta Park **Great Abington, Cambridge, United Kingdom** (Address of principal executive offices)	**CB21 6GS** (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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

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, 2025 (the last business day of the registrant's most recently completed second fiscal quarter) was $266,666,552.

As of March 12, 2026, the registrant had 50,269,082 ordinary shares, nominal value £0.01 per share, and 19,437,944 non-voting 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 2026 Annual General Meeting, 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, 2025, 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, or this Annual Report, contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements may be identified by such forward-looking terminology as "will," "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 pipeline programs for our Bicycle® Drug Conjugate, or BDC® molecules, and Bicycle Radioconjugates, or BRC® molecules, as well as 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, including communications with and feedback from the FDA and other regulatory agencies;
- 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;
- costs associated with defending intellectual property infringement, product liability and other claims;
- regulatory developments in the United States, the United Kingdom and other jurisdictions and changes to the laws and regulations of England and Wales, and other jurisdictions;
- estimates of our expenses, future revenues, capital requirements, share performance and our needs for additional financing;
- the potential benefits of strategic collaboration agreements and our ability to enter into additional strategic arrangements or partnership;
- 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 potential growth;
- our hiring plans and our ability to attract and retain qualified employees and key personnel;
- our estimates regarding expected future cost savings and charges associated with our strategic reprioritization and workforce reduction announced in March 2026;
- the impact of adverse global economic conditions, including those arising from changes in global trade policies, on our operations and the potential disruption in the operations and business of third-party manufacturers, contract research organizations, or CROs, other service providers, and collaborators with whom we conduct business;
- potential adverse developments affecting the financial services industry;
- potential business interruptions resulting from geo-political actions, such as war and terrorism, or the perception that such hostilities may be imminent;
- our failure or perceived failure to comply with existing or future laws, regulations, contracts, self-regulatory schemes, standards, and other obligations related to data privacy and security (including our ability to identify and respond to potential future security incidents); 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, 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. 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.

Unless the context otherwise requires, the terms "Bicycle," "the Company," "we," "our," "us" or similar references in this Annual Report refer to Bicycle Therapeutics plc and its subsidiaries.

TABLE OF CONTENTS

PART I

ITEM 1. BUSINESS.

We are a clinical-stage pharmaceutical company developing a novel class of medicines, which we refer to as Bicycle® molecules, for diseases that are underserved by existing therapeutics. Bicycle molecules are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making Bicycle molecules attractive candidates for drug development. Bicycle molecules 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 Bicycle molecules allows targets to be drugged that have historically been intractable to non-biological approaches. Bicycle molecules are excreted by the kidney rather than the liver and have shown no significant signs of immunogenicity to date, qualities which we believe explain the molecules' favorable toxicological profile.

We have a novel and proprietary phage display screening platform which we use to identify Bicycle molecules 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 quintillions of potential Bicycle molecules 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 internal programs are focused on oncology indications with high unmet medical need. Our product candidate, nuzefatide pevedotin, formerly BT5528, is a Bicycle Drug Conjugate, or a BDC® molecule, whereby the Bicycle molecule is chemically attached to a toxin that, when administered, is cleaved from the Bicycle molecule and kills the tumor cells. We are evaluating nuzefatide pevedotin, a BDC molecule targeting Ephrin type A receptor 2, or EphA2, in both an ongoing company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and clinical activity in patients with advanced solid tumors and an ongoing company-sponsored Phase II clinical trial to evaluate the efficacy, safety and pharmacokinetics of nuzefatide pevedotin in adult patients with recurrent metastatic pancreatic ductal adenocarcinoma after progression on a first-line therapy, which commenced recruiting patients in the first quarter of 2026. We are also developing BT1702, a Bicycle Radioconjugate, or BRC®, molecule targeting Membrane Type 1 matrix metalloproteinase, or MT1-MMP, and carrying a lead-212, or ^{212}Pb, radioisotope payload for theranostic use. We are currently conducting Investigational New Drug application, or IND, -enabling activities for BT1702. We are also developing Bicycle Imaging Agents, or BIA molecules. In a BIA molecule, a Bicycle molecule is linked to a chelated radiopharmaceutical imaging agent. We are using BIA molecules to potentially derisk novel targets prior to further clinical development and to efficiently triage cancer indications for subsequent treatment with both BRC and BDC molecules. Our discovery pipeline in oncology includes next-generation BDC molecules, BRC molecules and BIA molecules.

Zelenectide pevedotin, a BDC molecule targeting Nectin-4, is being evaluated in an ongoing company-sponsored Phase I/II clinical trial to assess the safety, pharmacokinetics and clinical activity in patients with Nectin-4 expressing advanced malignancies, an ongoing Phase II/III registrational trial called Duravelo-2 evaluating zelenectide pevedotin in patients with untreated and previously treated metastatic urothelial cancer and in ongoing company-sponsored Phase I/II clinical trials to assess the efficacy and safety of zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer, which commenced recruiting patients in the first and third quarters of 2025, respectively. In March 2026, we announced the strategic reprioritization of our clinical portfolio to focus on our promising pipeline of next-generation therapeutics, including nuzefatide pevedotin as well as next-generation Bicycle conjugates, including BRC molecules. While dose selection data from the clinical trial for zelenectide pevedotin are promising, demonstrating response rates comparable to published rates for existing standards of care and a differentiated safety profile, we plan to convert the Phase II/III Duravelo-2 registrational trial to a randomized Phase II clinical trial and deprioritize the program for internal development while we evaluate next steps for zelenectide pevedotin following preliminary feedback from regulatory agencies. In addition, as part of the strategic reprioritization, we plan to discontinue the Phase I/II clinical trials evaluating zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified

advanced or metastatic non-small cell lung cancer. Further enrollment in these trials will be closed and patients already enrolled will complete their course of treatment. In conjunction with our strategic reprioritization, we are implementing a proposed workforce reduction of approximately 30% of our workforce. Together, the workforce reduction and strategic reprioritization are expected to reduce our annual operating expenses by approximately 50% based on our current plans.

Our other product candidate, BT7480, is a Bicycle Tumor-Targeted Immune Cell Agonist®, or Bicycle TICA® molecule. A Bicycle TICA molecule links immune cell receptor binding Bicycle molecules to tumor antigen binding Bicycle molecules. BT7480, a Bicycle TICA molecule targeting Nectin-4 and agonizing CD137, is being evaluated in a company-sponsored Phase I/II clinical trial. After reporting certain data from the clinical trial in the first half of 2026, we will no longer develop BT7480 internally and intend to explore partnership opportunities for future development.

Beyond our wholly owned oncology portfolio, we are collaborating with biopharmaceutical companies and organizations in additional therapeutic areas in which we believe our proprietary Bicycle screening platform can identify therapies to treat diseases with significant unmet medical need.

The following table summarizes key information about our Bicycle programs:

Target	Molecule	Study	Indication	Preclinical	IND enabling/ human imaging	Early-Stage Development	Late-Stage Development
Internal oncology programs							
EphA2	**nuzefatide pevedotin (BDC®)**	Ph2 open label	PDAC				
		Ph1/2 combo with nivolumab	2L+ mUC				
	^{68}Ga BIA	Utility study	All comers				
MT1-MMP	**^{68}Ga BIA**	Utility study	All comers				
	BT1702 (BRC®, ^{212}Pb)	IND enabling	All comers				
Nectin-4	**zelenectide pevedotin (BDC®)**	**Duravelo-2** Ph2 combo with pembrolizumab	1L mUC				
			2L+ mUC				
	BT7480 (TICA®)	Ph1/2 combo with nivolumab	All comers				
Partnered programs							
PLN	**ION826/AZD4063**	Phase 1	Cardiometabolic disease				

1L: 1st line; 2L+: 2nd line or later; IND: Investigational New Drug; mUC: metastatic urothelial cancer; PDAC: pancreatic ductal adenocarcinoma; BIA: Bicycle® Imaging Agent; BDC®: Bicycle® Drug Conjugate: BRC®: Bicycle® Radioconjugate; TICA® : Bicycle tumor-targeted immune cell agonist®; PLN: phospholamban gene

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 Bicycle molecules. From our founding through December 31, 2025, we have generated substantial intellectual property, including eight patent families directed to novel scaffolds, linkers and payloads, eight patent families directed to our platform technology, 42 patent families directed to bicyclic peptides and related conjugates, and 16 patent families directed to later inventions relating to such bicyclic peptides and related conjugates, such as methods of making or using certain bicyclic peptide conjugates for treating various indications. As of December 31, 2025, our trademark portfolio consisted of 138 trademark registrations across 10 territories (United Kingdom, European Union, United States, Japan, Hong Kong, Australia, China, Israel, Switzerland and Norway) as well as a number of pending applications for new trademarks. The work we have conducted in developing Bicycle molecules and our proprietary screening platform have created substantial know-how that we believe provides us with a competitive advantage.

Our management team includes veteran executives in drug development from leading pharmaceutical companies including AstraZeneca, GlaxoSmithKline and Pfizer. Our board of directors, clinical advisory board and research and innovation advisory board include industry experts with extensive experience in drug development.

Our Strategy

Our mission is to become a leading pharmaceutical company by pioneering Bicycle molecules 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 internal candidate, nuzefatide pevedotin.*** We are evaluating nuzefatide pevedotin, a BDC molecule targeting EphA2, in both an ongoing company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and clinical activity in patients with advanced solid tumors and an ongoing company-sponsored Phase II clinical trial to evaluate the efficacy, safety and pharmacokinetics of nuzefatide pevedotin in adult patients with recurrent metastatic pancreatic ductal adenocarcinoma, which commenced recruiting patients in the first quarter of 2026.

- ***Progress IND-enabling activities for our BRC molecule candidate, BT1702.*** BT1702 is a theranostic BRC molecule targeting MT1-MMP and carries a ^{212}Pb radioisotope payload. In preclinical models, BT1702 showed a favorable biodistribution profile and was effective at reducing tumor burden in a range of model systems. IND-enabling activities are ongoing.

- ***Advance our discovery programs into clinical development.*** We intend to continue our ongoing discovery activities to screen and select candidates for oncology indications. For example, we are developing BRC molecules targeting novel targets, including EphA2. We have also provided our BIA molecules to German Cancer Research Center, or DKFZ, and Universitätsmedizin Essen for human imaging, which may inform future development. We intend to advance our Bicycle radioligands pipeline and progress our strategy for leadership in next-generation radiopharmaceuticals. We are also developing next generation BDC molecules.

- ***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 Bicycle molecules to increase diversity and confer differentiated physicochemical and structural properties. We have used our powerful Bicycle screening platform to identify BDC, BRC, BIA and Bicycle TICA molecules, and we 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. For example, in December 2025, ION826 (AZD4063), an investigational medicine incorporating a TfR1 Bicycle molecule under our collaboration agreement with Ionis, entered Phase I development. ION826 is an investigational siRNA medicine in development for a serious form of myocardial disease called PLN-R14del dilated cardiomyopathy. We may opportunistically enter into additional collaborations in the future to apply our technology to areas of unmet medical need.

- ***Maximize the commercial potential of our product candidates, if approved, 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.

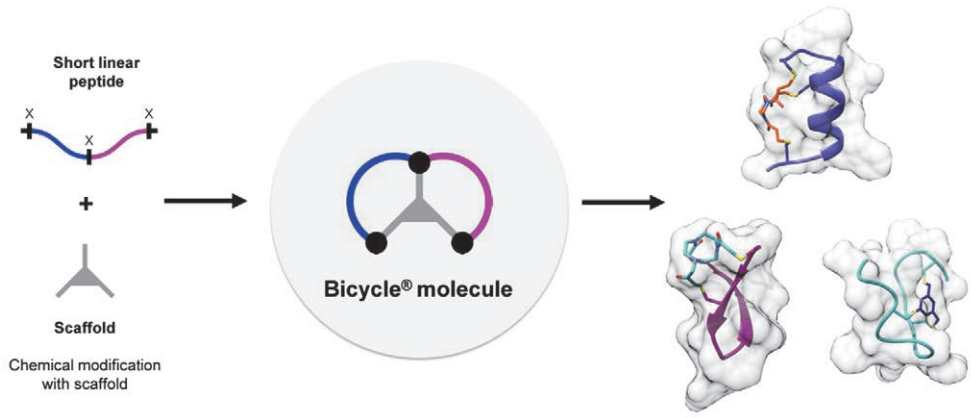
The Bicycle® Advantage

Introduction to Bicycle molecules

Bicycle molecules 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. Bicycle molecules 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 significant 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 molecule, is locked in the preferred state to bind to the target proteins.

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



We have expanded the diversity of the chemical space we can cover from approximately 10^{13} potential molecules in 2009 to in excess of 10^{20} potential molecules today. We have applied our novel Bicycle modality to a growing range of targets, from a single target in 2009 to more than 150 today. We can create a wide range of Bicycle molecules 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 molecule.

Properties of Bicycle Molecules as Therapeutic Agents

Bicycle molecules 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. Bicycle molecules 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 molecules, 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 Bicycle molecules allows us to optimize therapeutic molecules for specific targets.

Compared to biologics, Bicycle molecules have a lower cost of production and a simpler manufacturing process and are recognized by regulatory authorities as small molecule new chemical entities. We can readily identify Bicycle molecules that may 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 Bicycle molecules 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 with the historical average time being 12 months after a target has been selected.

Properties of Bicycle Molecules 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 structure found in native ligands ▸ Ability to generate diverse libraries covering a wide chemical space ▸ No significant 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 find to target classes usually intractable to small molecules 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 Bicycle Molecules to Other Common Classes of Therapeutics

	Bicycle	Antibody	ScFv (fragment)	Peptide	Small molecule
Molecular weight	~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	No significant signs to date	Possible	Frequent	Possible	None

* Requires use of extension technology

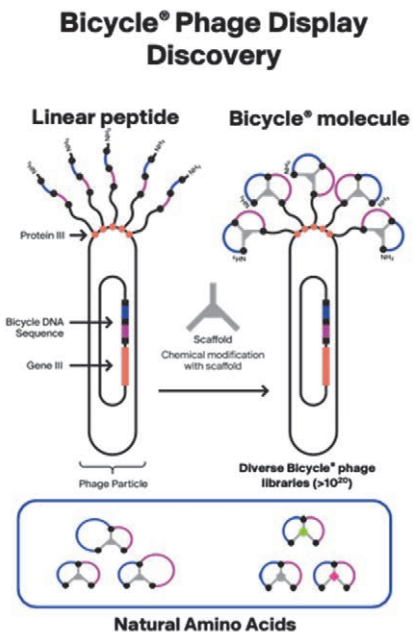
Our Proprietary Bicycle Screening Platform

We utilize our novel and proprietary phage display screening platform to identify Bicycle molecules 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.

Phage are bacteria-infecting viruses consisting of genetic material wrapped in a protein coat. Phages can be harnessed to identify Bicycle molecules by splicing DNA into the genome of a phage so that the linear peptides that encode Bicycle molecules are presented on the surface of the phage. One of our founders, Sir Greg Winter, a pioneer in phage display, applied this technology and added a cyclization step that forms Bicycle molecules from these linear peptides. This technology underpins our novel and proprietary screening platform.

Our screening process self-selects for Bicycle molecules that are amenable to attachment, commonly referred to as conjugation, to other molecular payloads such as cytotoxins, chelated radiopharmaceutical agents, innate immune agonists or other Bicycle molecules. Bicycle molecules can be linked together with synthetic ease to create complex molecules with combinatorial pharmacology. Alternatively, Bicycle molecules in the form of multimers can also be used as standalone therapeutics, such as those in our systemic and tumor-targeted immune cell agonist programs. We believe that the flexibility of our Bicycle molecules 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. We can readily identify Bicycle molecules that may 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.

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 150 challenging targets to date, successfully identifying Bicycle molecules for over 85% of these targets since our initial public offering, or IPO, some of which are intractable to small molecules. During these screens, Bicycle molecules 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 additional therapeutic areas where we believe our proprietary Bicycle screening platform can identify therapies to treat diseases with significant unmet medical need.

Our Programs

The following table summarizes key information about our programs.

Program	Interest	Stage	Status
Internal programs			
Nuzefatide pevedotin (EphA2)	• High EphA2 expressing tumors (oncology)	• Phase I/II	• Ongoing company-sponsored Phase I/II clinical trials
BT1702 (MT1-MMP BRC)	• Radiopharmaceutical	• IND enabling	• IND-enabling activities ongoing
MT1-MMP (BIA)	• Radiopharmaceutical	Human imaging	• Human imaging ongoing
EphA2 (BRC)	• Radiopharmaceutical	• Preclinical	• Lead optimization activities ongoing
EphA2 (BIA)	• Radiopharmaceutical	• Human imaging	• Human imaging ongoing
Zelenectide pevedotin (Nectin-4)	• High Nectin-4 expressing tumors (oncology)	• Phase II	• Evaluating next steps
BT7480 (Nectin-4/CD137)	• Immuno-oncology	• Phase I/II	• Exploring partnership opportunities
Partnered programs			
Novel CNS targets	• CNS	• Preclinical	• Collaborating with Ionis
Novel neuromuscular targets	• Neuromuscular	• Preclinical	• Collaborating with Ionis
ION826 (AZD4063)	• Cardiometabolic disease	• Phase I	• Collaborating with Ionis
Undisclosed	• Radiopharmaceutical	• Preclinical	• Collaborating with Bayer

Our Internal Programs

We believe Bicycle molecules are an ideal vehicle to deliver small molecule payloads to tumors, each as potent cytotoxins in the case of BDC molecules, chelated radiopharmaceutical payloads in the case of BRC molecules, chelated radiopharmaceutical imaging agents in the case of BIA molecules, as well as small molecule agonists of the immune system in the case of Bicycle TICA molecules. We believe that Bicycle conjugates can offer improved performance as compared to antibody-mediated delivery.

In addition to their use as drug conjugates, Bicycle molecules can also be configured for use as standalone therapeutics. We have identified Bicycle molecules that have been observed to directly interact with CD137, a key immune cell co-stimulatory molecule. We believe our CD137-targeting Bicycle molecules 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 Drug Conjugates

Within our BDC programs, we are evaluating nuzefatide pevedotin, a BDC molecule that targets EphA2 and carries an MMAE cytotoxin payload, in both an ongoing, company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics, and preliminary clinical activity in patients with solid tumors historically associated with EphA2 expression, as well as an ongoing, company-sponsored Phase II clinical trial to evaluate the efficacy, safety and pharmacokinetics of nuzefatide pevedotin in adult patients with metastatic pancreatic ductal adenocarcinoma. Nuzefatide pevedotin has also been granted Fast Track Designation, or FTD, for treatment of adult patients with previously treated, locally advanced or metastatic urothelial cancer. In addition, zelenectide pevedotin, a BDC molecule targeting Nectin-4, is being evaluated in an ongoing company-sponsored Phase I/II clinical trial to assess the safety, pharmacokinetics and clinical activity in patients with Nectin-4 expressing advanced malignancies, an ongoing Phase II/III registrational trial called Duravelo-2 evaluating zelenectide pevedotin in patients with untreated and previously treated metastatic urothelial cancer and in ongoing company-sponsored Phase I/II clinical trials to assess the efficacy and safety of zelenectide

pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer. In March 2026, we announced the strategic reprioritization of our clinical portfolio. As a result, we plan to convert the Phase II/III Duravelo-2 registrational trial to a randomized Phase II clinical trial and deprioritize the program for internal development while we evaluate next steps for zelenectide pevedotin and we plan to discontinue the Phase I/II clinical trials evaluating zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer.

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 on the surface. Finally, the relatively long systemic exposure and subsequent liver clearance generally associated with ADCs result in dose-limiting toxicities as well as other toxicities, such as hematological, liver, ocular, skin and gastrointestinal toxicities, and neuropathies.

Properties of Bicycle Drug Conjugates

We believe the properties of our BDC molecules 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.*** Bicycle molecules have been observed in our preclinical studies to penetrate tumors more rapidly and exhibit increased penetration to poorly perfused regions of the tumor when compared to a comparator antibody. Early clinical data from an ongoing clinical trial has shown 10 times higher tumor cytotoxin levels than corresponding plasma levels based on clinical tumor biopsies taken 24 hours post-infusion.

- ***Retention in tumors.*** In preclinical studies, following administration of a tumor antigen targeting Bicycle molecule the toxin payload was observed to be retained in the tumor for at least 120 hours after dosing. Preliminary clinical data observed to date from our ongoing clinical trials are consistent with preclinical observations of post-dose tumor retention.

- ***Short systemic half-life and renal elimination***. Bicycle molecules have been observed in clinical and preclinical studies to have a short systemic half-life of approximately 20 to 30 minutes. Due to their small size, Bicycle molecules 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, BDC molecules do not require internalization into the cell, and therefore potentially can target a wider range of tumor antigens.

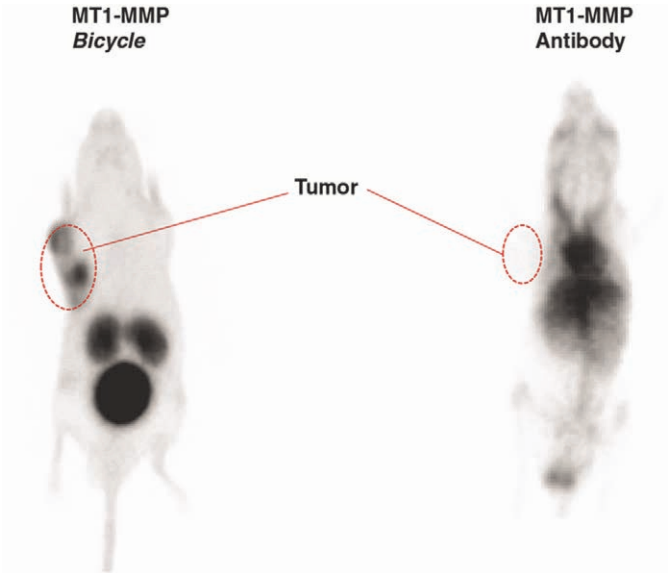
- ***Access to non-expressing tumor cells.*** The toxin in our BDC molecules is liberated in the extracellular space, enabling cell-killing adjacent cells that do not express the specific target through a toxin bystander effect. In our preclinical studies, we observed activity for BDC molecules even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

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

- ***Manufacturing.*** The fully synthetic process by which Bicycle molecules 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 molecule 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 molecule 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 Bicycle molecules in the bladder and kidneys, indicating rapid renal excretion. In contrast, the antibody was detected in the vasculature.

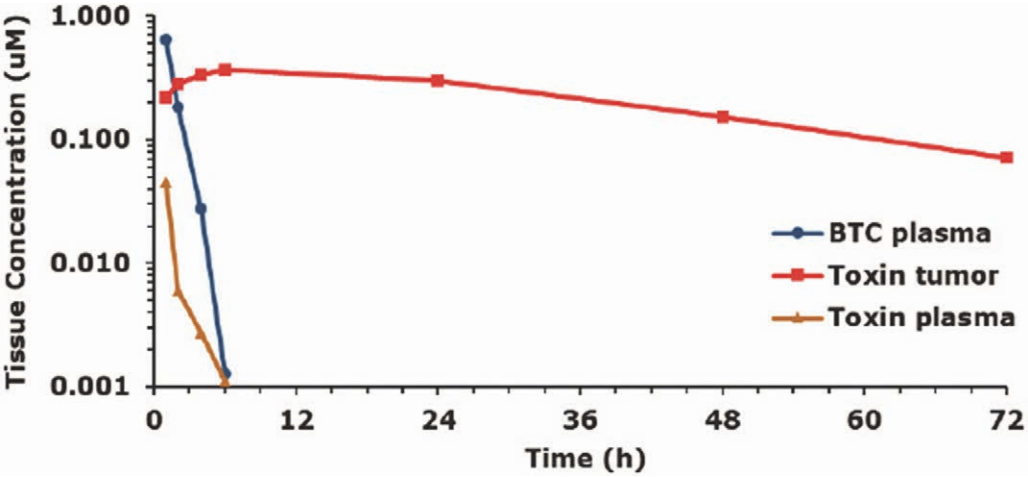
PET Imaging Revealing Payload Delivery in a Mouse Model



In addition, in a preclinical rodent study using photoacoustic imaging, we observed that Bicycle molecules 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 BDC molecule. 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 BDC Molecule

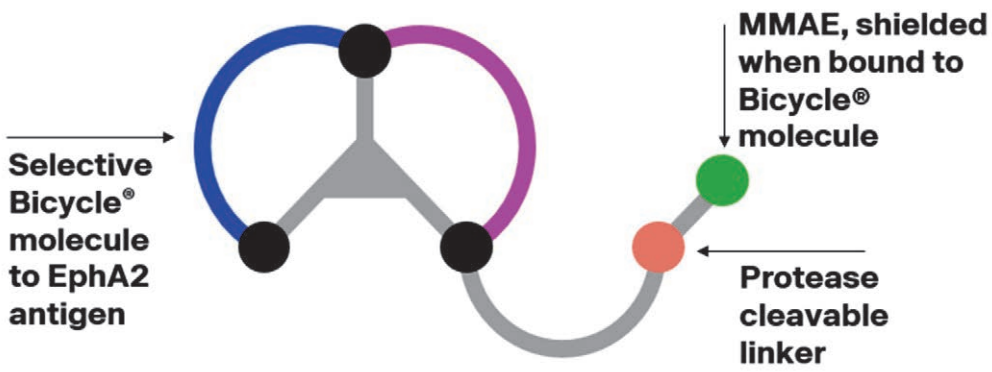


We believe these data demonstrate the potential of BDC molecules to have long-term sustained activity and to limit the toxicity associated with ADCs.

Nuzefatide pevedotin

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

Schematic of Nuzefatide Pevedotin



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, head and neck, gastric, ovarian, and pancreatic cancer. 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.

EphA2 has been pursued by other companies utilizing antibody drug conjugates, or ADCs. 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 enzymes 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 BDC molecules due to the potential of Bicycle molecules to overcome the safety concerns observed with ADCs. In our preclinical PK and toxicokinetic studies, we observed a short systemic half-life and volume of distribution approximately equal to extracellular fluid. 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 nuzefatide pevedotin could overcome the challenges faced by ADCs.

Nuzefatide pevedotin was evaluated in preclinical studies in multiple species, including rodents and non-human primates. In our preclinical studies, nuzefatide pevedotin 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.

Clinical Development

We are currently evaluating nuzefatide pevedotin in an ongoing company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and preliminary clinical activity in patients with advanced solid tumors historically associated with EphA2 expression. Nuzefatide pevedotin has been granted FTD for treatment of adult patients with previously treated, locally advanced or metastatic urothelial cancer.

In September 2024, we announced updated Phase I/II clinical results for nuzefatide pevedotin in advanced solid tumors, including metastatic urothelial cancer and ovarian cancer, at the ESMO Congress 2024. Updated results from the ongoing Phase I/II clinical trial evaluating 6.5 mg/m^2 every two weeks and 5 mg/m^2 weekly of nuzefatide pevedotin monotherapy in patients with advanced solid tumors showed an ORR of 12% among 113 efficacy-evaluable patients with advanced solid tumors. Of these, the highest anti-tumor activity was in metastatic urothelial cancer, with a 34% ORR in all efficacy-evaluable patients enrolled in the dose escalation and expansion cohorts. Among patients receiving 6.5 mg/m^2 every two weeks, a 31% ORR was observed in the dose escalation and expansion cohort and a 45% ORR was observed in the expansion cohort only. A lower, but acceptable ORR of 27% was observed in patients receiving 5 mg/m^2 weekly. There were no objective responses observed in patients with ovarian cancer who received 5 mg/m2 weekly. However, five patients maintained stable disease at the time of data cut off. In addition, the updated results suggested a correlation between EphA2 expression and response. Among 14 patients with metastatic urothelial cancer who had available immunohistochemistry and response data, a 43% ORR was observed in EphA2-positive patients compared to a 20% ORR in EphA2-negative patients.

Nuzefatide pevedotin showed an emerging differentiated safety profile, with none of the hemorrhage events or hematological toxicities that have been associated with other EphA2-targeting drug conjugates. Low rates of treatment-related peripheral neuropathy, or TRPN, were observed following monotherapy treatment with nuzefatide pevedotin. In 74 patients treated with nuzefatide pevedotin at 6.5 mg/m^2 every two weeks, results showed TRPN in 19% of patients, nearly all of which were low grade, with no events at or above Grade 3. TRPN had completely resolved in 21% of nuzefatide pevedotin patients, and 21% had some resolution or improvement at the time of reporting, though post-treatment follow-up was limited. The median time to resolution or improvement of TRPN was 1.7 weeks for nuzefatide pevedotin.

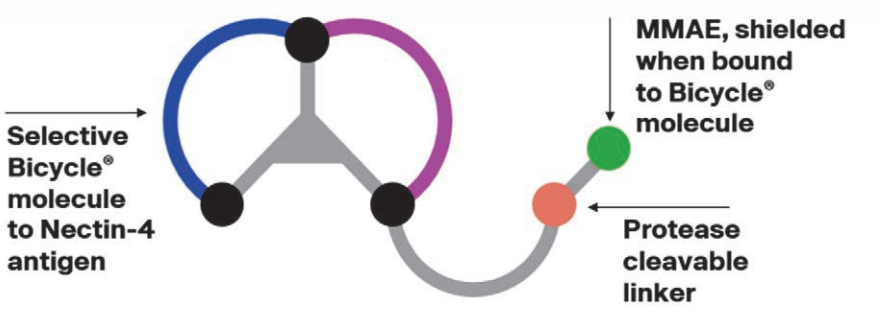
We are currently assessing nuzefatide pevedotin at 6.5 mg/m^2 every two weeks in combination with nivolumab and are further evaluating nuzefatide pevedotin in certain other tumor indications. We plan to present data for nuzefatide pevedotin in combination with nivolumab in patients with metastatic urothelial cancer at a scientific conference in the first half of 2026.

We are also evaluating nuzefatide pevedotin in a company-sponsored Phase II clinical trial to evaluate the efficacy, safety and pharmacokinetics of nuzefatide pevedotin in adult patients with recurrent metastatic pancreatic ductal adenocarcinoma, which commenced recruiting patients in the first quarter of 2026. Additional information regarding this indication will be presented at a scientific conference in the first half of 2026.

Zelenectide Pevedotin

Zelenectide pevedotin is a BDC molecule designed to target Nectin-4, a well-validated tumor antigen. The molecule is composed of our Nectin-4 targeting *Bicycle* molecule, a val-cit cleavable linker, and a cytotoxin MMAE payload.

Schematic of Zelenectide Pevedotin



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 December 2019, the U.S. Food and Drug Administration, or the FDA, granted accelerated approval to enfortumab vedotin, a Nectin-4 ADC program developed jointly by Pfizer Inc. (formerly Seagen, Inc., or Seagen, acquired by Pfizer in December 2023) and Astellas Pharma, Inc., or Astellas, for treatment of locally advanced or metastatic urothelial cancer in patients who had received prior PD-1/PD-L1 and platinum-based therapies. In July 2021, enfortumab vedotin received full approval in this setting as well as a label expansion for patients ineligible to receive cisplatin-containing therapy who received prior lines of therapy. Subsequently, enfortumab vedotin in combination with pembrolizumab has been approved in the locally advanced or metastatic setting for cisplatin-ineligible patients in April 2023 and all locally advanced or metastatic patients in December 2023. The most recent approval for this combination came in December 2025 for neoadjuvant treatment followed by continued adjuvant therapy after cystectomy for patients with muscle-invasive bladder cancer, or MIBC, who are ineligible for cisplatin-based chemotherapy. Starting in 2022, enfortumab vedotin, alone or in combination with pembrolizumab, has received similar approvals/incorporation into clinical consensus guidelines for indications in the locally advanced and metastatic settings in major markets outside of the United States.

Clinical Development

Zelenectide pevedotin, a BDC molecule targeting Nectin-4, is being evaluated in an ongoing company-sponsored Phase I/II clinical trial to assess the safety, pharmacokinetics and clinical activity in patients with Nectin-4 expressing advanced malignancies, an ongoing Phase II/III registrational trial called Duravelo-2 (which we plan to convert to a randomized Phase II trial) evaluating zelenectide pevedotin in patients with untreated and previously treated metastatic urothelial cancer and in ongoing company-sponsored Phase I/II clinical trials to assess the efficacy and safety of zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer, which commenced recruiting patients in the first and third quarters of 2025, respectively. Zelenectide pevedotin has been granted FTD by the FDA as a monotherapy for the treatment of adult patients with previously treated, locally advanced or metastatic urothelial cancer. Zelenectide pevedotin has also been selected to participate in the Chemistry, Manufacturing and Controls, or CMC, Development and Readiness Pilot Program launched by the FDA to facilitate CMC development for therapies with expedited clinical development timeframes based on the anticipated clinical benefits of earlier patient access to the therapy.

In September 2024, we announced updated Phase I/II clinical results for zelenectide pevedotin used as a monotherapy in metastatic urothelial cancer at the European Society for Medical Oncology, or ESMO, Congress 2024. In the ongoing Phase I/II clinical trial evaluating 5 mg/m^2 weekly of zelenectide pevedotin monotherapy in 45 metastatic urothelial cancer patients who had not previously been treated with enfortumab vedotin, updated results showed an overall response rate, or ORR, of 45% in 38 efficacy-evaluable patients, including one confirmed complete response and 16 partial responses with 13 confirmed. Stable disease was maintained in nine patients, and 12 patients experienced progressive disease. In addition, updated results showed a median duration of response of 11.1 months among the 14 patients with confirmed responses. Zelenectide pevedotin continued to show an emerging differentiated safety profile, particularly around adverse events of interest such as peripheral neuropathy, skin reactions and eye disorders. Notably, there were no treatment-related adverse events of peripheral neuropathy, skin reactions or eye disorders at or above Grade 3, and patients with pre-existing peripheral neuropathy were unlikely to develop worsening peripheral neuropathy during treatment with zelenectide pevedotin. In addition, low rates of TRPN were observed following monotherapy treatment with zelenectide pevedotin. In 149 patients treated with zelenectide pevedotin, results showed TRPN in 28% of patients, nearly all of which were low grade. One Grade 3 event of neuralgia was reported in a patient treated with zelenectide pevedotin following prior therapy with enfortumab vedotin. Among zelenectide pevedotin patients with peripheral neuropathy at baseline, 80% did not develop TRPN during treatment. TRPN had completely resolved in 14% of zelenectide pevedotin patients and 26% had some resolution or improvement at the time of reporting, though post-treatment follow-up was limited. The median time to resolution or improvement of TRPN was 2.2 weeks for zelenectide pevedotin.

In January 2025, we also announced updated topline results from the ongoing Phase I trial evaluating 5 mg/m^2 weekly of zelenectide pevedotin plus 200 mg of pembrolizumab once every three weeks. In 22 previously untreated cisplatin-ineligible patients with metastatic urothelial cancer, results showed an ORR of 65% among all 20 efficacy-evaluable patients, and an ORR of 50% among patients with confirmed responses. Of the three unconfirmed responses, one patient remained on treatment. At the time of the data cut, the median duration of response was not yet mature, with 12 patients still on treatment. The safety and tolerability profile continues to be broadly consistent with other Phase I zelenectide pevedotin monotherapy and combination cohorts. Adverse events of interest such as peripheral neuropathy, skin reactions and eye disorders were primarily low grade. All cases of Grade 3 treatment-related adverse events of interest were reversible, and there were no Grade 4 or Grade 5 treatment-related adverse events of interest.

We plan to present longer-term follow-up data for zelenectide pevedotin used as a monotherapy in late-line metastatic urothelial cancer and additional data for zelenectide pevedotin in combination with pembrolizumab in first-line cisplatin-ineligible and cisplatin-eligible metastatic urothelial cancer at a scientific conference in the first half of 2026.

In March 2026, we announced the strategic reprioritization of our clinical portfolio to focus on our promising pipeline of next-generation therapeutics, including nuzefatide pevedotin as well as next-generation Bicycle conjugates, including BRC molecules. While dose selection data from the Phase II/III Duravelo-2 clinical trial are promising, we plan to convert the Phase II/III Duravelo-2 registrational trial to a randomized Phase II clinical trial and deprioritize the

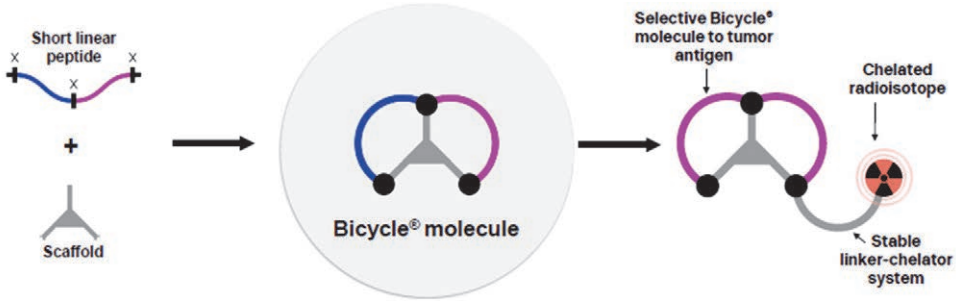
program for internal development while we evaluate next steps for zelenectide pevedotin following preliminary feedback from regulatory agencies. Initial dose selection data from the Phase II/III Duravelo-2 clinical trial demonstrate response rates comparable with those published for existing standards of care, with a physician assessed ORR of 65%, a blinded independent central review, or BICR, confirmed ORR of 58% at the 27-week cutoff and a differentiated safety profile. Subsequent to the 27-week cutoff, an additional BICR response was observed, which would result in an ORR of 62%. The 6mg dose demonstrated a differentiated safety profile with only one patient discontinuing therapy due to a treatment-related adverse event at the 27-week cutoff. We plan to report initial dose selection data from the Duravelo-2 trial at a future scientific conference.

In addition, as part of the strategic reprioritization, we plan to discontinue the Phase I/II clinical trials evaluating zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer. Further enrollment in these trials will be closed and patients already enrolled will complete their course of treatment.

Bicycle Radioligands Pipeline

Radiopharmaceuticals are therapies that contain radioisotopes and are used in nuclear medicine for the diagnosis and treatment of diseases, particularly cancer. They consist of radioactive isotope (radionuclide) combined with a pharmaceutical agent that targets specific organs or tissues. These agents are used for molecular imaging (PET/SPECT) or targeted therapy to destroy cancer cells. To create radiopharmaceuticals, radiation emitting medical isotopes are typically attached through chelation to targeting molecules, which are then administered via intravenous injection. Once administered, the radiopharmaceuticals are designed to target tumor antigens that are unique to, or preferentially expressed on, cancer cells. We believe the same advantages of Bicycle molecules for selectively delivering cytotoxic payloads are also advantageous for delivering a range of diverse radionuclide payloads. We are developing both BRC molecules for theranostic use as well as BIA molecules which we are using to potentially derisk novel targets prior to further clinical development and to efficiently triage cancer indications for subsequent treatment with both BRC and BDC molecules.

Schematic of Proposed Bicycle Radioligand Molecules



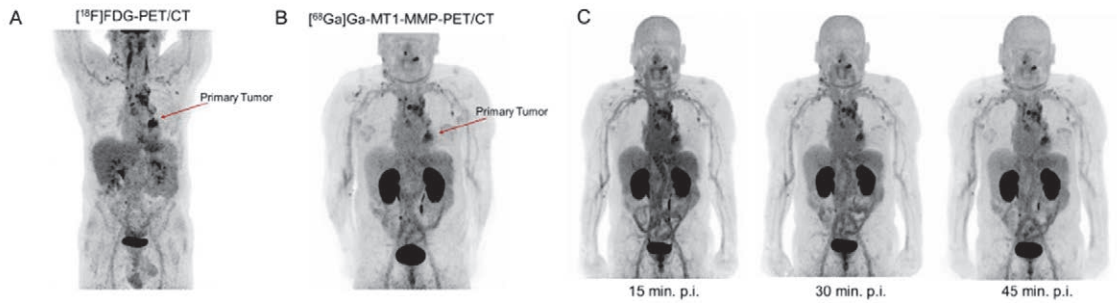
Bicycle molecules have ideal properties for radioisotope delivery due to their low molecular weight lending to rapid extravasation and tumor penetration, high selectivity and high affinity for their intended target, sustained tumor retention and rapid systemic clearance. Our strategy for radiopharmaceuticals involves (i) partnering with industry and academic leaders in the radiopharmaceutical field to build our understanding and deepen our knowledge base, (ii) pursuing novel targets with first-in-class potential by using BIA molecules to potentially derisk targets through human imaging and to direct indication selection for subsequent treatment with both BRC and BDC molecules and (iii) studying our BRC and BIA molecules with a range of isotopes to pair the most appropriate with the application, target biology and indication.

Manufacturing challenges and ensuring supply chain continuity and reliability have historically hindered the development and commercialization of radiopharmaceuticals. To overcome these challenges, we have established arrangements with leading isotope suppliers and manufacturers for a potentially world-leading end-to-end and sustainable radioisotope supply chain. For instance, we have established an agreement with Eckert & Ziegler, a leading

isotope technology company, to supply a range of radioisotopes and develop and manufacture BRC and BIA molecules. In addition, in December 2025, we announced our entrance into a 15-year contract, including an option to renew, with the UK Nuclear Decommissioning Authority, or UKNDA, for access to up to 400 tonnes of reprocessed uranium. Reprocessed uranium continually regenerates providing a potentially sustainable supply of lead-212, or ^{212}Pb, a radioisotope and one of the more potent therapeutic payloads against cancer cells known as Targeted Alpha Therapy. We also announced a collaboration with United Kingdom National Nuclear Laboratory, or UKNNL, pursuant to which we plan to extract thorium-228, or ^{228}Th, from the reprocessed uranium obtained from UKNDA. The extracted ^{228}Th will then be further processed into radium-224, or ^{224}Ra, and loaded into ^{212}Pb generators currently being developed exclusively for us by SpectronRx, with whom we have an agreement to develop bespoke ^{212}Pb generators, with initial quantities of ^{212}Pb successfully produced. Collectively, we believe this bespoke set of arrangements is designed to support the potential discovery, development and commercial supply of a portfolio of BRC molecules containing ^{212}Pb.

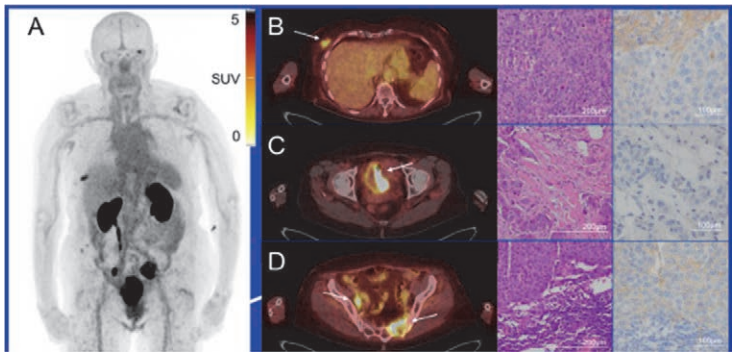
We are developing a pipeline of novel Bicycle molecules with properties which we have optimized using our proprietary approach for radioisotope delivery. In October 2024, first human imaging data for a BIA molecule targeting MT1-MMP, which was not optimized to minimize kidney retention, was presented by the German Cancer Consortium, or DKTK, part of a cooperative network with DKFZ, at the European Association for Nuclear Medicine, or EANM, 2024 Congress and in April 2025, DKTK presented additional human imaging data at the American Association for Cancer Research, or AACR, Annual Meeting 2025. The images presented were of a 65-year old male diagnosed with advanced pulmonary adenocarcinoma, the most common type of non-small cell lung cancer, and an 84-year old female diagnosed with invasive ductal breast cancer and high-grade urothelial cancer.

The 65-year old male patient with advanced pulmonary adenocarcinoma underwent fluorine-18-labelled FDG-PET/CT imaging and two weeks later underwent MT1-MMP PET/CT imaging up to one hour post injection of the gallium-68-labelled BIA tracer.



The MT1-MMP gallium-68 scan demonstrated uptake in the primary tumor in the lung and in the lymph node and other metastases, corroborating the findings of the FDG scan. While the MT1-MMP gallium-68 scan demonstrated lower uptake in the primary tumor compared to the FDG imaging (maximum standardized uptake value, or SUVmax, 6.0 g/mL vs. 10.3 g/mL), MT1-MMP gallium-68 uptake was comparable in lymph node metastases (SUVmax 4.7 g/mL vs. 4.4 g/mL) and higher in bone metastases (SUVmax 7.9 g/mL vs. 6.0 g/mL).

The 84-year old female patient with invasive ductal breast cancer and high-grade urothelial cancer underwent contrast-enhanced CT imaging and later underwent MT1-MMP gallium-68 PET/CT imaging up to one hour post injection of the gallium-68-labelled BIA tracer.



The MT1-MMP gallium-68 scan revealed higher BIA tracer uptake in the primary tumors in the breast (SUVmax 4.5 g/mL) and the bladder (SUVmax 6.6 g/mL) compared to contrast-enhanced CT imaging. The MT1-MMP scan also showed cancer spread to the lymph nodes, lower spine (sacral bone) and skull, and detected a mass in the adrenal gland above the left kidney. Surgery confirmed the patient had bladder cancer that spread to the lymph nodes, and immunohistochemistry testing confirmed MT1-MMP expression in the tumor cells.

These data are representative of the results seen in 12 out of 14 patients with various cancers, including those affecting the lung, head and neck, and bladder, who have undergone MT1-MMP gallium-68 PET imaging to date. Imaging was unsuccessful or inconclusive in two patients. Overall, the results demonstrate the rapid distribution of the BIA tracer throughout the body, high uptake of the BIA tracer in the primary tumor(s) and/or in metastases where the cancer spread in the body, and elimination through the kidneys. Scans showing retention in the kidneys were in line with expectations given the imaging was conducted using a pathfinder BIA molecule which had not been optimized to minimize kidney retention. Additional and more detailed analyses of the data and confirmation of MT1-MMP expression in tumors via immunohistochemistry are ongoing.

In addition, at the EANM 2024 Congress, we presented preclinical data demonstrating the suitability of Bicycle molecules to deliver indium-111 to tumors *in vivo* due to their favorable properties, including specific tumor uptake, rapid tumor penetration and rapid renal elimination. Preclinical imaging showed how the biodistribution profile of BRC molecules can be optimized to maintain high tumor uptake and retention while significantly reducing kidney uptake and retention.

Altogether, we believe these data validate the potential of MT1-MMP as a novel target in the treatment of cancer, demonstrate the translatability of Bicycle radioligand preclinical data and highlight the potential of Bicycle molecules for targeted radionuclide therapy.

Outside of MT1-MMP, we have selected a novel tumor antigen EphA2 as our second Bicycle radioligand target. In November 2025, we presented first human imaging data for an early BIA molecule targeting EphA2 at the Targeted Radiopharmaceuticals Summit Europe, supporting the potential of EphA2 as a novel cancer target and further demonstrating the attractive properties of Bicycle molecules for radiopharmaceutical applications. We plan to present additional EphA2 human imaging data in the first half of 2026.

BT1702

BT1702 is a theranostic BRC molecule targeting MT1-MMP and carries a ^{212}Pb radioisotope therapeutic payload. In preclinical models, BT1702 showed a favorable biodistribution profile and was effective at reducing tumor burden in a range of model systems. IND-enabling activities for BT1702 are currently ongoing. We plan to initiate the first company-sponsored radioligand clinical trial for BT1702 in 2027.

Bicycle Tumor-Targeted Immune Cell Agonists

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 Bicycle molecules may allow us to develop molecules with a pharmacodynamically distinct and improved profile over existing therapies.

BT7480

BT7480, a Bicycle TICA molecule targeting Nectin-4 and agonizing CD137, is being evaluated as a monotherapy and in combination with nivolumab in a company-sponsored Phase I/II clinical trial to assess the safety and tolerability of BT7480, and to determine a recommended Phase II dose.

In September 2024, we announced updated Phase I/II clinical trial results for BT7480 in advanced solid tumors at the ESMO Congress 2024. Initial data from the dose escalation portion of the Phase I/II clinical trial evaluating BT7480 in patients with advanced solid tumors showed an emerging differentiated safety and tolerability profile among 39 patients assigned to receive one of 10 different doses of BT7480, ranging from 0.002-3.5 mg/kg weekly, with a low number of severe adverse events. Low rates of adverse events at or above Grade 3 were observed, with 8% of patients experiencing treatment-related adverse events at or above Grade 3 and 5% of patients experiencing treatment-related severe adverse events at or above Grade 3. No such events were observed among those patients receiving the highest dose of 3.5 mg/kg. The best overall response observed was stable disease in 13 patients, five of whom had non-small cell lung cancer. Stable disease was prolonged in three patients, two with non-small cell lung cancer and one with anal cancer. In addition, there were two unconfirmed partial responses, both in patients with cervical cancer. Preliminary biomarker analyses that support BT7480 dual targeting of CD137 and Nectin-4 as demonstrated by enhanced immune cell activation, aligned with the proposed mechanism of action of BT7480.

We plan to present data from the combination cohort at a scientific conference in the first half of 2026. After reporting combination data in the first half of 2026, we will no longer develop BT7480 internally and intend to explore partnership opportunities for future development.

Our Collaborations

Beyond our wholly owned oncology portfolio, we are collaborating with biopharmaceutical companies and organizations in additional therapeutic areas in which we believe our proprietary Bicycle screening platform can identify therapies to treat diseases with significant unmet medical need by leveraging the broad applicability of Bicycle molecules. Our strategic collaborations are based on the ability of Bicycle molecules to address a wide variety of targets and we are working with collaborators with deep therapeutic expertise to enable us to more efficiently develop novel medicines for patients. For additional information on these collaboration agreements, see Note 9. “Significant agreements” of our consolidated financial statements appearing elsewhere in this Annual Report.

Bayer

On May 4, 2023, we entered into a collaboration and license agreement with Bayer Consumer Care AG, or Bayer, pursuant to which we and Bayer will perform research and discovery activities under a mutually agreed upon research plan during a research term up to a specified number of years per target program to generate radiopharmaceutical compounds incorporating optimized Bicycle constructs directed to two specified targets, under the oversight of a joint research committee. In addition, Bayer has a one-time right to expand the collaboration to include a third target program, and with respect to each of the up to three target programs, Bayer has an option, exercisable within a specified period of time following the effective date of the agreement, to generate, develop and commercialize non-radiopharmaceutical compounds directed to the applicable target, either by itself or in collaboration with us. Bayer also has certain limited target substitution rights, in certain cases subject to specified additional payments. For each collaboration program, Bayer may elect, at its sole discretion, to progress compounds arising from activities under the research programs into further preclinical development of potential products directed to the target of such collaboration program. On a target-by-target basis, if Bayer elects to progress development candidates directed to such target into further clinical development, Bayer will be required to use commercially reasonable efforts to develop and seek regulatory approval in certain major markets for products directed to the applicable target. In November 2025, Bayer

provided the Company with a notice of termination for one of the initial target programs, with such termination to be effective in January 2026.

Ionis

On July 9, 2021, we and Ionis entered into a collaboration and license agreement, or the Ionis Collaboration Agreement. Pursuant to the Ionis Collaboration Agreement, we granted to Ionis a worldwide exclusive license under our relevant technology to research, develop, manufacture and commercialize products incorporating Bicycle peptides directed to the protein coded by the gene TFRC1 (transferrin receptor), or TfR1 Bicycle molecules, intended for the delivery of oligonucleotide compounds directed to targets selected by Ionis for diagnostic, therapeutic, prophylactic and preventative uses in humans. Ionis will maintain exclusivity to all available targets unless it fails to achieve specified development diligence milestone deadlines. If Ionis fails to achieve one or more development diligence milestone deadlines, we have the right to limit exclusivity to certain specific collaboration targets, subject to the payment by Ionis of a low-single-digit million dollar amount per target as specified in the Ionis Collaboration Agreement. Each party was responsible for optimization of such TfR1 Bicycle molecules and other research and discovery activities related to TfR1 Bicycle molecules, as specified by a research plan which was completed during 2024, and thereafter Ionis is responsible for all future research, development, manufacture and commercialization activities. We performed research and discovery activities including a baseline level of effort for a period of three years. We have retained certain rights, including the right to use TfR1 Bicycle molecules for all non-oligonucleotide therapeutic purposes. In December 2025, ION826 (AZD4063), an investigational medicine incorporating a TfR1 Bicycle molecule under the Ionis Collaboration Agreement, entered Phase I development. ION826 is an investigational siRNA medicine in development for a serious form of myocardial disease called PLN-R14del dilated cardiomyopathy.

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, composition of matter of bicyclic peptides identified through use of the platform and further chemical optimization, conjugates comprising such bicyclic peptides, methods of using our product candidates, and other inventions that are important to our business.

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, or USPTO. 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.

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

Company-Owned Intellectual Property

As of December 31, 2025, our patent portfolio included eight patent families directed to novel scaffolds, linkers and payloads, eight patent families directed to our platform technology, 42 patent families directed to bicyclic peptides and related conjugates, and 16 patent families directed to later inventions relating to such bicyclic peptides and related conjugates, such as methods of making or using certain bicyclic peptide conjugates for treating various indications.

We own at least eight patent families relating to our product candidate nuzefatide pevedotin, including patent families directed to its composition of matter, methods of use for treating cancer and methods of identifying patients suitable to receive nuzefatide pevedotin. The issued patents in these families, and the pending patent applications if issued, are expected to expire between 2038 and 2044, not including any patent term extensions and/or patent term adjustments.

We own at least 12 patent families relating to our product candidate zelenectide pevedotin, including patent families directed to its composition of matter, methods of use for treating cancer, synthetic routes to zelenectide pevedotin and methods of identifying patients suitable to receive zelenectide pevedotin. The issued patents in these families, and the pending patent applications if issued, are expected to expire between 2039 and 2045, not including any patent term extensions and/or patent term adjustments.

We own at least 10 patent families relating to our product candidate BT7480, including patent families directed to its composition of matter and the composition of matter of its constituent bicyclic peptides, methods of use for treating cancer, combinations with other active agents, and the methods of identifying patients suitable to receive BT7480. The issued patents from these families, and the pending patent applications, if issued, are expected to expire between 2038 and 2044, not including any patent term extensions and/or patent term adjustments.

In total, as of December 31, 2025, we owned about 536 patents in the United States and in foreign jurisdictions, such as Australia, Canada, China, Europe, Hong Kong, Japan, New Zealand, Russia and Singapore. In addition, as of December 31, 2025, we had about 412 patent applications pending in the United States and in foreign jurisdictions, such as Argentina, Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Korea, New Zealand, Russia, Singapore and Taiwan, as well as pending international applications under the Patent Cooperation Treaty, or PCT. These patents, as well as any patents that may be issued from these patent applications, are generally expected to have terms that will expire at various dates between February 2029 and August 2045, not including any patent term extensions and/or patent term adjustments.

In total, as of December 31, 2025, we owned 138 trademark registrations across 10 territories (United Kingdom, European Union, United States, Japan, Hong Kong, Australia, China, Israel, Switzerland and Norway), as well as a number of pending applications for new trademarks.

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 companies are developing programs for the targets, including Nectin-4 and EphA2, that we are exploring for our BDC programs, including, but not limited to, Pfizer Inc. (formerly Seagen, acquired by Pfizer Inc. in December 2023) which has a marketed Nectin-4 antibody-drug conjugate, Eli Lilly and Company, Mabwell Therapeutics, Inc., Tianjin Conjustar Biologics Co., Ltd. and Stemline Therapeutics. Furthermore, many companies are developing programs for radiopharmaceutical therapies. 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 our 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 and Supply

Each of our Bicycle molecules is entirely synthetic. We believe the synthetic nature of our product candidates allows for a more cost effective and scalable manufacturing process compared to biologics. In addition, this property of Bicycle molecules 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 Bicycle molecules can be made to be well controlled, reproducible and scalable.

We currently do not own or operate good manufacturing practice, or GMP, manufacturing facilities and we operate an outsourced model for the manufacture of our product candidates, and contract with multiple GMP licensed pharmaceutical contract development and manufacturing organizations, both for the synthesis of each drug substance component, and the formulation and packaging of finished drug product candidates. We selected these organizations based on their experience, capability, capacity and regulatory status. 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.

We engage with third parties for the supply of radioisotopes for the development and manufacturing of BRC and BIA molecules. For instance, we've established an agreement with Eckert & Ziegler, a leading isotope technology company, to supply a range of radioisotopes and develop and manufacture BRC and BIA molecules. In addition, in December 2025, we entered into a contract with UKNDA for access to up to 400 tonnes of reprocessed uranium. We also entered into an arrangement with UKNNL under which we plan to extract ^{228}Th from the reprocessed uranium obtained from UKNDA. The extracted ^{228}Th will then be further processed into ^{224}Ra, and loaded into ^{212}Pb generators currently being developed exclusively for us by SpectronRx, with whom we have an agreement to develop bespoke ^{212}Pb generators, with initial quantities of ^{212}Pb successfully produced. Collectively, we believe this bespoke set of arrangements is designed to support the potential discovery, development and commercial supply of a portfolio of BRC molecules containing ^{212}Pb.

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 10 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 NDA 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 an application under rolling review 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 and to provide regular updates to the FDA on the progress of such studies. 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.

Chemistry, Manufacturing, and Controls Development and Readiness Pilot (CDRP) Program

In October 2022, the FDA announced a two-year opportunity for a limited number of applicants to participate in the CDRP program to facilitate expedited development CMC development of products under an IND, where warranted, based on the anticipated clinical benefit of earlier patient access to the products. The FDA has implemented this pilot program to facilitate CMC readiness for selected Center for Biologics Evaluation and Research, or CBER, and Center for Drug Evaluation and Research, or CDER, regulated products with accelerated clinical development timelines. To accelerate CMC development and facilitate CMC readiness, the pilot features increased communication between the FDA and sponsors and explores the use of science- and risk-based regulatory approaches, such as those described in FDA guidance, as applicable.

Project Optimus

Project Optimus is an initiative of the Oncology Center of Excellence at the FDA. This project focuses on dose optimization and dose selection in oncology drug development, and whether the current paradigm based on cytotoxic chemotherapeutics leads to doses and schedules of molecularly targeted therapies that provide more toxicity without additional efficacy, among other things. In Project Optimus, drug developers have the opportunity to meet with the FDA's Oncology Review Divisions early in their development programs, well before conducting trials intended for registration, to discuss dose-finding and dose optimization. The program thus allows sponsors to develop strategies for dose finding and dose optimization that leverages nonclinical and clinical data in dose selection, including randomized evaluations of a range of doses in trials, with the objective of performing these studies as early as possible in the development program to bring new therapies to patients.

Project Frontrunner

Project Frontrunner is an Oncology Center of Excellence initiative to encourage drug sponsors to consider when it may be appropriate to first develop and seek approval of new cancer drugs for advanced or metastatic disease, in an earlier clinical setting rather than the usual approach to develop and seek approval of a new drug for treatment of patients who have received numerous prior lines of therapies or have exhausted available treatment options. The goals of Project Frontrunner are to develop a framework for identifying candidate drugs that are appropriate to initially develop for the treatment of early metastatic disease (e.g., first or second line setting), taking into account clinical, scientific, regulatory and operational considerations; facilitate engagement with drug sponsors during drug development to develop and implement strategies to support approvals in early clinical setting; and to engage and collaborate with internal and external stakeholders on related research, policy and educational initiatives.

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 Drug Supply Chain Security Act, which regulates the distribution of drugs at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states, which additionally limit the distribution of prescription pharmaceutical products 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. 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. 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.

European Union/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.

Clinical Trials in the EU

In the European Union, or EU, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014, or CTR, which entered into application on January 31, 2022 repealing and replacing the former Clinical Trials Directive 2001/20, or CTD. The CTR foresaw a three-year transition period that ended on January 31, 2025. Since this date, all new or ongoing trials are subject to the provisions of the CTR.

The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase transparency. Specifically, the Regulation, which is directly applicable in all EU Member States, introduces a streamlined application procedure through a single-entry point, the "EU portal," the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is led by the competent authorities of a reference Member State selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU Member States. This assessment is then submitted to the competent authorities of all concerned Member States in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and Ethics Committees in each concerned EU Member State. Individual EU Member States retain the power to authorize the conduct of clinical trials on their territory.

In all cases, clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Medicines used in clinical trials must be manufactured in accordance with the guidelines on cGMP and in a GMP licensed facility, which can be subject to GMP inspections.

EU Review and Approval Process

In the EU, medicinal products can only be commercialized after a related marketing authorization, or MA, has been granted. To obtain an MA for a product in the EU, an applicant must submit a Marketing Authorization Application, or MAA, either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by the competent authorities of EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid throughout the European Economic Area, or EEA (which is comprised of the 27 EU Member States plus Norway, Iceland and Liechtenstein). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs, and (iv) products with a new active

substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval.

Under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, conducts the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. The maximum timeframe for the evaluation of an MAA under the centralized procedure is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product targeting an unmet medical need is expected to be of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts a request for accelerated assessment, the time limit of 210 days will be reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralised Procedures – Human, or CMDh, for review. The subsequent decision of the European Commission is binding on all EU Member States.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the MA of a medicinal product by the competent authorities of other EU Member States. The holder of a national MA may submit an application to the competent authority of an EU Member State requesting that this authority recognize the MA delivered by the competent authority of another EU Member State.

An MA has, in principle, an initial validity of five years. The MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the Common Technical Document providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five-year renewal period for the MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicinal products that target unmet medical needs. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicinal product will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Benefits accrue to sponsors of product candidates with PRIME designation,

including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted.

In the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization; (iii) the medicinal product fulfils an unmet medical need; and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and must be renewed annually until all related conditions have been fulfilled. Once any pending studies are provided, the conditional MA can be converted into a traditional MA. However, if the conditions are not fulfilled within the timeframe set by the EMA and approved by the European Commission, the MA will cease to be renewed.

An MA may also be granted "under exceptional circumstances" where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. These circumstances may arise in particular when the intended indications are very rare and, in the state of scientific knowledge at that time, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Like a conditional MA, an MA granted in exceptional circumstances is reserved to medicinal products intended to be authorized for treatment of rare diseases or unmet medical needs for which the applicant does not hold a complete data set that is required for the grant of a standard MA. However, unlike the conditional MA, an applicant for authorization in exceptional circumstances is not subsequently required to provide the missing data. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually, and the MA will be withdrawn if the risk-benefit ratio is no longer favorable.

Pediatric Development in the EU

In the EU, Regulation (EC) No 1901/2006 provides that all MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the medicinal product for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures provided in the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU Member States and study results are included in the product information, even when negative, the product is eligible for a six-month extension to the Supplementary Protection Certificate, or SPC, if any is in effect at the time of authorization or, in the case of orphan medicinal products, a two-year extension of orphan market exclusivity.

Manufacturing Regulation in the EU

In addition to an MA, various other requirements apply to the manufacturing and placing on the EU market of medicinal products. The manufacturing of medicinal products in the EU requires a manufacturing authorization and import of medicinal products into the EU requires a manufacturing authorization allowing for import. The manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including EU cGMP standards. Similarly, the distribution of medicinal products within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of EU Member States. Marketing authorization holders and/or manufacturing and import authorization, or MA holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing

authorization, in case of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

Data and Market Exclusivity in the EU

The EU provides opportunities for data and market exclusivity related to MAs. Upon receiving an MA, innovative medicinal products are generally entitled to receive eight years of data exclusivity and 10 years of market exclusivity. Data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar MAA can be submitted, and the innovator's data may be referenced. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall ten-year period may, occasionally, be extended for a further year to a maximum of 11 years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical/biological entity, and products may not qualify for data exclusivity.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product. For such products, the results of appropriate preclinical or clinical trials must be provided in support of an application for MA. Guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product.

Orphan Designation in the EU

In the EU, Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (ii) either (a) such conditions affect not more than 5 in 10,000 persons in the EU when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product. An application for the designation of a medicinal product as an orphan medicinal product must be submitted at any stage of development of the medicinal product but before filing of an MAA. An MA for an orphan medicinal product may only include indications designated as orphan. For non-orphan indications treated with the same active pharmaceutical ingredient, a separate marketing authorization has to be sought.

Orphan medicinal product designation entitles an applicant to incentives such as fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of 10 years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product designation, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal

product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar medicinal product with the same orphan indication during the 10 year period if: (i) if the applicant consents to a second original orphan medicinal product application; (ii) if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities; or (iii) if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A company may voluntarily remove a product from the register of orphan products.

Post-Approval Requirements in the EU

Where an MA is granted in relation to a medicinal product in the EU, the holder of the MA is required to comply with a range of regulatory requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the individual EU Member States. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk- minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

Other EU Compliance Requirements

In the EU, the advertising and promotion of medicinal products are subject to both EU and EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. General requirements for advertising and promotion of medicinal products, such as direct-to-consumer advertising of prescription medicinal products are established in EU law. However, the details are governed by regulations in individual EU Member States and can differ from one country to another. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, which may require approval by the competent national authorities in connection with an MA. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU.

Much like the federal Health Care Program Anti-Kickback Statute, or Anti-Kick Statute, prohibition in the United States, described above, the provision of benefits or advantages to physicians and other health care professionals to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. Interactions between pharmaceutical companies and healthcare professionals are governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. Infringement of related laws could result in substantial fines or imprisonment.

Payments made to physicians and other healthcare professionals in certain EU Member States must be publicly disclosed. Moreover, agreements with healthcare professionals may require prior notification or approval by the healthcare professional's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Regulation of Companion Diagnostics in the EU

In the EEA, companion diagnostics are deemed to be *in vitro* diagnostic medical devices, or IVDs, and are governed by Regulation 2017/746, or IVDR, which entered into application on May 26, 2022, repealing and replacing Directive 98/79/EC. The IVDR defines a companion diagnostic as a device which is essential for the safe and effective use of a corresponding medicinal product to: (a) identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or (b) identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product.

The IVDR and its associated guidance documents and harmonized standards govern, among other things, device design and development, preclinical and clinical or performance testing, premarket conformity assessment, registration and listing, manufacturing, labeling, storage, claims, sales and distribution, export and import and post-market surveillance, vigilance, and market surveillance. IVDs, including companion diagnostics, must conform with the general safety and performance requirements, or GSPR, of the IVDR. Compliance with these requirements is a prerequisite to be able to affix the CE mark to devices, without which they cannot be marketed or sold in the EEA. To demonstrate compliance with the GSPR laid down in Annex I to the IVDR, and obtain the right to affix the CE mark, IVD manufacturers must conduct a conformity assessment procedure, which varies according to the type of IVD and its classification. Apart from low risk IVDs (Class A which are not sterile), in relation to which the manufacturer may issue an EU Declaration of Conformity based on a self-assessment of the conformity of its products with the GSPRs, a conformity assessment procedure requires the intervention of a Notified Body, which is an organization designated by a Competent Authority of an EEA country to conduct conformity assessments. Depending on the relevant conformity assessment procedure, the Notified Body audits and examines the technical documentation and the quality system for the manufacture, design and final inspection of the medical devices. The Notified Body issues a CE Certificate of Conformity following successful completion of a conformity assessment procedure conducted in relation to the medical device and its manufacturer and their conformity with the GSPRs. This Certificate and the related conformity assessment process entitles the manufacturer to affix the CE mark to its medical devices after having prepared and signed a related EC Declaration of Conformity.

Companion diagnostics must undergo a conformity assessment by a Notified Body. If the related medicinal product has, or is in the process of, been authorised through the centralized procedure for the authorization of medicinal products, the notified body will, before it can issue a CE Certificate of Conformity, be required to seek a scientific opinion from the EMA on the suitability of the companion diagnostic for use in relation to the medicinal product concerned. For medicinal products that have or are in the process of authorisation through any other route provided in EU legislation, the Notified Body must seek the opinion of the national competent authority of an EU Member State.

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, products 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. Our results of operations could be adversely affected by healthcare legislative reforms, including those that may be enacted or adopted in the future. For example, the U.S. Department of Health and Human Services, or HHS, imposes rebates on many Medicare Part B and Medicare Part D products to penalize price increases that outpace inflation on an annual basis. HHS has also been empowered to negotiate the price of certain single-source drugs that have been on the market for at least seven years covered under Medicare as part of the Medicare Drug Price Negotiation Program. Each year up to 20 products will be selected by HHS for the Medicare Drug Price Negotiation Program. Products subject to the Medicare Drug Price Negotiation Program are expected to experience a significant reduction in reimbursement from the Medicare program on a per unit basis. 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. 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. In addition, some EU Member States may require the completion of additional studies that compare the cost-effectiveness of a particular medicinal product candidate to currently available therapies. This Health Technology Assessment, or HTA, process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. 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, health information privacy and security, price reporting and physician sunshine laws. Some of our pre-commercial activities are subject to some of these laws.

The 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 or another business associate, and their covered subcontractors. 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, annual reporting requirements for covered manufacturers for certain payments and other transfers of value provided to physicians, as defined by such law, other healthcare professionals (such as physician assistant and nurse practitioners), and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family members.

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.

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. The ACA, which was signed into law in 2010, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Since its enactment, there have been amendments and judicial and Congressional challenges to numerous provisions of the ACA. For example, on July 4, 2025, the One Big Beautiful Bill Act, or the OBBBA, was signed into law, which narrowed access to ACA marketplace exchange enrollment and declined to extend the ACA enhanced advanced premium tax credits that expired at the end of 2025, which, among other provisions in the law, are anticipated to reduce the number of Americans with health insurance. The OBBBA also is expected to reduce Medicaid spending and enrollment by implementing work requirements for some beneficiaries, capping state-directed payments, reducing federal funding, and limiting provider taxes used to fund the program. Congress is considering proposed legislation intended to further reduce healthcare costs with alternatives to replace the expired ACA subsidies. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregated reductions to Medicare payments to providers of 2% per fiscal year, which began in 2013 and will remain in effect through 2032 unless additional Congressional action is taken.

The current administration is pursuing policies to reduce regulations and expenditures across government agencies, including at HHS, the FDA, Centers for Medicare and Medicaid Services, or CMS, and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. For example, the current administration has announced agreements with several pharmaceutical companies that require the drug manufacturers to offer, through a direct-to-consumer platform, U.S. patients and Medicaid programs prescription drug Most-Favored-Nation pricing equal to or lower than those paid in other developed nations, with additional mandates for direct-to-patient discounts and repatriation of foreign revenues. Other recent actions, for example, include (1) directing agencies to reduce agency workforce and cut programs; (2) directing HHS and other agencies to lower prescription drug costs through a variety of initiatives, including by improving upon the Medicare Drug Price Negotiation Program and establishing Most-Favored-Nation pricing for pharmaceutical products; (3) imposing tariffs on imported pharmaceutical products; and (4) as part of the Make America Healthy Again Commission's Strategy Report released in September 2025, working across government agencies to increase enforcement on direct-to-consumer pharmaceutical advertising. Additionally, the current administration recently called on Congress to enact "The Great Healthcare Plan," to codify and expand Most-Favored-Nation pricing, lower government subsidies to private insurance companies, increase healthcare price transparency, expand pharmaceutical drugs available for over-the-counter purchase, and enact restrictions on pharmacy benefit manager payment methodologies, among other things. These actions and policies may significantly reduce U.S. drug prices, potentially impacting manufacturers' global pricing strategies and profitability, while increasing their operational costs and compliance risks. Congress may introduce and ultimately pass healthcare-related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

In addition, on January 12, 2025, Regulation No 2021/2282 on HTA, or the HTA Regulation, entered into application through a phased implementation. The HTA Regulation initially applies to new active substances for oncology and ATMPs. It will be expanded to orphan medicinal products in January 2028, and to all centrally authorized medicinal products as of 2030. Select high-risk medical devices also came into scope in 2026. The HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products. The HTA Regulation establishes a framework for EU-level joint clinical assessments, joint scientific

consultations, and the early identification of emerging health technologies. The HTA Regulation permits EU Member States to use common tools, methodologies, and procedures and requires them to rely on EU-level joint clinical assessment reports for the clinical components of their national HTA evaluations. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies and pricing and reimbursement decisions based on these assessments.

There have been, and likely will continue to be, healthcare reform measures, including 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.

Regulatory Framework in the United Kingdom

The Medicines and Healthcare products Regulatory Agency, or the MHRA, is the United Kingdom's standalone regulator for medicinal products and medical devices.

While the United Kingdom's regulatory framework for clinical trials was historically based on the Medicines for Human Use (Clinical Trials) Regulations 2004, which implemented the former EU Clinical Trials Directive, this has been significantly reformed by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2024. The new legislation, which was adopted in April 2025, modernizes the United Kingdom's approach to make it a more attractive location for research, and includes key features such as: (i) a risk-proportionate approach, including a notification scheme for lower-risk trials; (ii) a combined review process integrating ethics committee and regulatory approvals into a single, streamlined pathway; (iii) enhanced transparency requirements mandating registration of clinical trials in a public registry and publication of trial results within 12 months of trial completion (with scope for deferrals in certain circumstances); (iv) greater flexibility to support innovation in clinical trial design; and (v) measures to promote patient and public involvement. The amendments will become applicable on April 28, 2026 following a one-year transition period.

Marketing authorizations in the United Kingdom are governed by the Human Medicines Regulations (SI 2012/1916), as amended. In order to obtain a United Kingdom marketing authorization, or MA, to commercialize products in the United Kingdom, an applicant must be established in the United Kingdom and must follow one of the United Kingdom national authorization procedures or one of the remaining post-Brexit international cooperation procedures. Applications are governed by the Human Medicines Regulations (SI 2012/1916) and are made electronically through the MHRA Submissions Portal. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, a 150-day assessment (subject to clock-stops) and a rolling-review procedure. The rolling-review procedure permits the separate or joint submission of quality, non-clinical and clinical data to the MHRA which can be reviewed on a rolling basis. After an application under the rolling-review procedure has been validated, the decision should be received within 100 days (subject to clock-stops).

In addition, since January 1, 2024, the MHRA may rely on the International Recognition Procedure, or IRP, when reviewing certain types of MAAs. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (e.g., the regulatory authorities in Australia, Canada, Switzerland, Singapore, Japan, the United States and the EU). The MHRA will conduct a targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. The IRP allows medicinal products approved by such trusted regulatory partners that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update a MA in the United Kingdom. Applications should be decided within a maximum of 60 days if: (i) there are no major objections identified that cannot be resolved within such 60-day period and (ii) approval from the trusted regulatory partner selected has been granted within the previous two years. Where major objections are identified or such approval has not been granted within the previous two years, the decision timeline extends to 110 days. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals.

Existing EU marketing authorizations for centrally authorized products were automatically converted into the United Kingdom's marketing authorizations, effective in Great Britain only, free of charge on January 1, 2021, unless the marketing authorization holder opted out of this possibility. On January 1, 2025, the Windsor Framework came into effect, reintegrating Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products and introducing a United Kingdom-wide licensing process for medicines.

There is no pre-marketing authorization orphan designation for medicinal products in the United Kingdom. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding marketing authorization application. The criteria are essentially the same as those in the EU, but have been tailored for the market. This includes the criterion that prevalence of the condition in the United Kingdom, rather than the EU, must not be more than five in 10,000. Upon the grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication. The start of this market exclusivity period will be set from the date of first approval of the product in the United Kingdom.

Employees and Human Capital

As of December 31, 2025, we had 288 full-time or part-time employees, including 108 with M.D. or Ph.D. degrees. Of these employees, 220 employees are engaged in research and development activities and 68 employees are engaged in general and administrative activities. Our employees are primarily based at the locations of our office and laboratory facilities: 191 are located in the United Kingdom and 97 are located in the United States. 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. In conjunction with our strategic reprioritization announced in March 2026, we are implementing a proposed workforce reduction of approximately 30% of our workforce.

Our human capital resources objectives include, as applicable, identifying, recruiting, developing, retaining, incentivizing and integrating our existing and additional employees to support the continued growth of our company and progress the development of our product candidates. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of equity-based compensation awards.

We believe a diverse workforce is critical to our success and we are fundamentally committed to creating and maintaining a work environment in which employees are treated fairly, with dignity, decency, respect and in accordance with all applicable laws. We understand that varied perspectives lead to the best ideas and outcomes. We believe that by creating a workplace where every individual can feel welcome and valued, we will be better able to achieve our corporate objectives. All employees must adhere to a code of business conduct and ethics and our employee handbook, which combined, define standards for appropriate behavior and all employees are annually trained to help prevent, identify, report, and stop any type of discrimination and harassment. Our processes in recruitment, hiring, development, training, compensation, and advancement are based on qualifications, performance, skills, and experience without regard to gender, race, or ethnicity.

Compensation and Benefits

We believe our employees are our most valuable assets and are key to achieving our goals. We focus our efforts on attracting and retaining a diverse, high-performing workforce through offering competitive and fair compensation packages that are based on robust industry market data. Our total compensation package includes competitive base pay, annual bonus, equity participation, and a broad range of benefits, including retirement planning, healthcare and insurance benefits, paid time off, enhanced paid family and medical leave, flexible working, and various health and wellness programs. We also run recognition programs that highlight employees who exhibit exceptional performance and demonstrate our company values.

We ensure that our compensation programs are designed to be equitable and fair, and routinely analyze data to ensure that our programs are administered in a fair and equitable way.

Career Development

We invest heavily in our employees' personal and professional development. We offer a vast array of learning and development opportunities including online and classroom training and learning, technical training, mentoring and coaching programs, training academies and management and leadership development programs.

We are committed to developing the next generation of talent and have active internship partnerships with local universities in both the United States and United Kingdom.

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, United Kingdom and one of which is based in Massachusetts, United States, that carry on our business.

The U.K. subsidiaries are BicycleTx Limited and BicycleRD Limited, and the U.S. subsidiary is Bicycle Therapeutics Inc. Our principal executive offices are located at Blocks A & B, Portway Building, Granta Park, Great Abington, Cambridge, CB21 6GS, 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 Reports 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 or any other report we file with or furnish to the SEC.

Item 1A. Risk Factors.

Our operations and financial results are subject to various risks and uncertainties, including those described below. The following information about these risks and uncertainties, together with the other information appearing elsewhere in this Annual Report on Form 10-K, or this Annual Report, including our consolidated financial statements and related notes thereto, should be carefully considered before a decision to invest in our American Depositary Shares, or 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.

Summary of Selected Risk Factors

Our business is subject to numerous risks and uncertainties, of which you should be aware before making a decision to invest in our ADSs. These risks and uncertainties include, among others, the following:

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

- 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.

- 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 are substantially dependent on the success of our internal development programs and of our product candidates from our Bicycle® Drug Conjugate, or BDC®, and Bicycle Radioconjugate, or BRC®, programs, which may not successfully complete clinical trials, receive regulatory approval or be successfully commercialized.

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

- We may 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.

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

- 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, or IND, that could halt their clinical development, prevent their marketing approval, limit their commercial potential or result in significant negative consequences.

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

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

- We may seek designations for our product candidates with the U.S. Food and Drug Administration, or 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.

- 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 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.

- 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.

- 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 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.

- 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, could limit our ability to market those products and decrease our ability to generate revenue.

- Healthcare legislative reform measures may have a negative impact on our business and results of operations.

- We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our (and third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, and other adverse business consequences.

- 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 intend to rely on third parties to manufacture product candidates and supply raw materials used in our product candidates, such as ^{212}Pb, 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.

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

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

- Our recent workforce reductions were undertaken to significantly reduce our ongoing operating expenses, but they may not result in our intended outcomes and may yield unintended consequences and additional costs.

- 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.

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

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 net losses of $219.0 million, $169.0 million and $180.7 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $899.8 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 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 BDC and BRC 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 current and former research collaborations with Bayer Consumer Care AG, or Bayer, Novartis Pharma AG, or Novartis, Ionis Pharmaceuticals, Inc., or Ionis, and Genentech Inc., or Genentech. There can be no assurance that we will generate revenue from our 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 pharmaceutical 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. 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 ongoing 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 and cash equivalents of $628.1 million as of December 31, 2025, 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. 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 and associated costs as we progress 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.

While the long-term economic impact of geopolitical risks, including evolving impacts from tariffs, sanctions or other trade tensions between the United States and other countries, or demand or supply shocks from events such as major terrorist attacks, war, natural disasters or actual or threatened public health pandemics or other emergencies is difficult to assess or predict, these events have caused or may cause significant disruptions to the global financial markets and have contributed or may contribute to a general global economic slowdown. Furthermore, inflation rates, particularly in the United States and the United Kingdom, recently increased to levels not seen in decades and, despite recent decreases, remain high. Increased inflation may result in increased operating costs (including labor costs) and may affect our operating budgets. Future increases in interest rates, especially if coupled with reduced government spending and volatility in financial markets and the global banking system, may further increase economic uncertainty and heighten these risks.

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 BDC and BRC 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 BDC and BRC programs.

Within our BDC programs, we are evaluating nuzefatide pevedotin, formerly BT5528, a BDC molecule that targets Ephrin type-A receptor 2, or EphA2 and carries a MMAE cytotoxin payload, in an ongoing, company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and preliminary clinical activity in patients with advanced malignancies historically associated with EphA2 expression as well as an ongoing, company-sponsored Phase II clinical trial to evaluate the efficacy, safety and pharmacokinetics of nuzefatide pevedotin in adult patients with recurrent metastatic pancreatic ductal adenocarcinoma. In addition, IND-enabling activities are currently ongoing for BT1702, a theranostic BRC molecule targeting MT1-MMP and carrying a ^{212}Pb radioisotope payload. There can be no assurance our BDC or BRC molecules will ever demonstrate evidence of safety or effectiveness for any use or receive regulatory approval in the United States, the European Union, or any other country in any indication. Even if clinical trials show positive results, there can be no assurance that the FDA in the United States, or the European Commission, whose decision is based on an opinion from the EMA in Europe or similar regulatory authorities will approve our BDC or BRC molecules 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 BDC molecules, BRC molecules, and our other product candidates will depend on, among other things, our ability to:

- successfully complete preclinical studies and clinical trials, which may be delayed;
- receive regulatory approvals from the FDA, the European Commission based on an opinion from 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 and maintain freedom to operate for such products with respect to the intellectual property rights of third parties.

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 or comparable foreign applications to competent regulatory authorities abroad, 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.

In addition, the policies of the FDA, the competent authorities of the EU Member States, the EMA, the European Commission and other comparable regulatory authorities responsible for clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The CTR, which was adopted in April 2014 and repeals the CTD, became applicable on January 31, 2022. The CTR introduces, among other changes, a centralized application system, coordinated review procedures, expanded reporting and increased transparency obligations. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

In addition, on December 11, 2025, the European Commission, European Parliament and European Council reached a political agreement on a comprehensive overhaul of EU pharmaceutical legislation, or the Pharma Package. The reform has been under negotiation since the European Commission submitted its proposal in April 2023. This package, composed of a new directive and regulation to replace existing legislation, aims to modernize the EU framework. The political agreement is still subject to formal approval by the European Parliament and European Council. If approved in the form proposed, the Pharma Package will, among other changes, reduce the baseline market protection period by one year, with limited opportunities for extensions; reshape the incentives regime for orphan medicinal products; and expand the Bolar exemption. A decrease in market exclusivity opportunities for our product candidates in the EU, combined with the expanded Bolar exemption, could open them to generic or biosimilar competition earlier than under the current regime, potentially impacting reimbursement status and the commercial prospects of our product candidates.

Moreover, following a public consultation that began in 2022, the United Kingdom government has enacted new legislation to overhaul the clinical trials regulatory framework. In April 2025, the United Kingdom adopted an amendment to the Medicines for Human Use (Clinical Trials) Regulations 2004 intended to support a more streamlined

and flexible regulation of clinical trials, remove unnecessary administrative burdens on trial sponsors, and protect the interests of trial participants. It also intends to bring the U.K. regulatory framework for clinical trials into closer alignment with the EU's CTR. The amendment will become applicable on April 28, 2026 following a one-year transition period. While these changes introduce efficiencies and align with some principles of the CTR, divergence between the United Kingdom and EU regulatory systems remains. Any significant divergence could affect the cost and complexity of conducting clinical trials in the United Kingdom and may impact the acceptability of United Kingdom-based trial data for seeking marketing authorizations in the EU, and vice versa.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, our development plans may be impacted.

We are at an early stage in our development efforts, and 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.

Bicycle molecules are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making Bicycle molecules attractive candidates for drug development. Bicycle molecules 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. 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 have limited experience with Bicycle molecules 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 the European Commission 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 European Commission based on a positive opinion from the EMA, or national competent regulatory authorities in the EEA, countries and any other comparable regulatory authorities in other jurisdictions must approve 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 European Commission based on a positive opinion from 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. New or ongoing public health crises may also impact our and our collaboration partners' abilities to activate trial sites or enroll patients in clinical trials or to otherwise advance those clinical trials. Interruptions resulting from such

crises may reduce our, or our collaboration partners', abilities to administer the investigational product to enrolled patients, present difficulties for enrolled patients to adhere to protocol-mandated visits and laboratory/diagnostic testing, increase the possibility of patient dropouts, or impact our, and our suppliers', abilities to provide investigational product to trial sites, all of which could negatively impact the data we are able to obtain from our clinical trials and complicate regulatory review.

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 the European Commission 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, inferior or a rigorous comparison cannot be made 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 the European Commission or other relevant regulatory authorities 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 our product candidates generally is performed in multiple jurisdictions, including countries 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 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 preliminary or 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 interim results of our company-sponsored Phase I/II clinical trials of nuzefatide pevedotin, zelenectide pevedotin and BT7480, including specific patient responses we have observed and disclosed, may not be replicated in the completed data sets or 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 late-stage 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, our ability to enroll trial participants, 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 or certification prior to commercialization. In the EEA (and Northern Ireland), in order to place an in vitro diagnostic medical device on the market, the device must be designed, developed, manufactured and marketed in compliance with the Regulation on In-Vitro Diagnostic Devices (Regulation (EU) 2017/746), which is a lengthy and costly process.

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 or certification 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 or certification 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 or certification 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 or difficulties obtaining insurance coverage and reimbursement from private insurance or government payors. 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. If unacceptable side effect profiles arise, or side effects beyond those identified to date develop or worsen, as we continue development of our current or future 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 Safety Review Committees 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, cause delays in ongoing clinical trials, 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.

Three of our product candidates are currently undergoing safety testing in the form of Phase I/II or Phase II/III 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 nuzefatide pevedotin, zelenectide pevedotin, BT7480 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 be delayed or 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 development strategy, product candidate or indication and fail to capitalize on strategies, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

In March 2026, we announced the strategic reprioritization of our clinical portfolio to focus on our promising pipeline of next-generation therapeutics, including nuzefatide pevedotin as well as next-generation Bicycle conjugates, including BRC molecules. While dose selection data from the Phase II/III Duravelo-2 clinical trial for zelenectide pevedotin are promising, demonstrating response rates comparable to published rates for existing standards of care and a differentiated safety profile, we plan to convert the Phase II/III Duravelo-2 registrational trial to a randomized Phase II

clinical trial and deprioritize the program for internal development while we evaluate next steps for zelenectide pevedotin following preliminary feedback from regulatory agencies. In addition, as part of the strategic reprioritization, we plan to discontinue the Phase I/II clinical trials evaluating zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer. Further enrollment in these trials will be closed and patients already enrolled will complete their course of treatment.

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 past resource allocation decisions, and those we may make in the future, 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 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. The EMA has a similar program called PRIME.

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 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.

Changes in the regulatory landscape, policies, or processes, as well as disruptions at the FDA and other government agencies caused by layoffs, changes in personnel, funding shortages or global health concerns could negatively impact our business.

The ability of the FDA to review proposed clinical trials or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, including executive and congressional priorities, the impacts of which are inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may slow the time necessary for new product candidates to be reviewed and/or approved, which would adversely affect our business. For example, over the last several years, including in October 2025, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions,

which could have a material adverse effect on our business. In addition, the current administration has implemented substantial reductions in force at various government agencies including the FDA, which could significantly reduce the FDA's capacity to perform its functions in a manner consistent with its past practices and could delay reviews and negatively impact our business. There is also increased uncertainty as to how the FDA and other regulatory agencies will regulate our products.

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 authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. It is possible that we could experience delays in the timing of our interactions with regulatory authorities due to absenteeism by governmental employees, inability to conduct planned physical inspections related to regulatory approval, or the diversion of regulatory authority efforts, which could delay anticipated approval decisions and otherwise delay or limit our ability to make planned regulatory submissions or obtain new product approvals. 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 authority policy during the period of product development, clinical trials and the review process. Any marketing approval we ultimately obtain, if any, 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 trial. 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 authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, regulatory authorities 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 limited 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 limited 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 build our 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 building 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 our failure to educate physicians on the benefits of prescribing our products;
- 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 expanding 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, third-line or later-line therapies, 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 nuzefatide pevedotin 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 or comparable foreign regulatory authorities may also require a Risk Evaluation and Mitigation Strategy, or REMS, or a comparable foreign strategy, 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 or comparable foreign regulatory authorities 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. Similar considerations apply outside of the United States.

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 or comparable foreign regulatory authorities 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 are 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 companies are developing programs for the targets, including Nectin-4 and EphA2, that we are exploring for our BDC programs, including, but not limited to, Pfizer Inc. (formerly Seagen, acquired by Pfizer Inc. in December 2023) which has a marketed Nectin-4 antibody-drug conjugate, Eli Lilly and Company, Mabwell Therapeutics, Inc., Tianjin Conjustar Biologics Co., Ltd. and Stemline Therapeutics. Furthermore, many companies are developing programs for radiopharmaceutical therapies.

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, EU 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 candidates 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 pharmaceutical 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, is 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 CMS 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.

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 drugs. For example, HHS imposes rebates on many Medicare Part B and Medicare Part D products to penalize price increases that outpace inflation on an annual basis. HHS has also been empowered to negotiate the price of certain single-source drugs that have been on the market for at least seven years covered under Medicare as part of the Medicare Drug Price Negotiation Program. Each year up to 20 products will be selected by HHS for the Medicare Drug Price Negotiation Program. Products subject to the Medicare Drug Price Negotiation Program are expected to experience a significant reduction in reimbursement from the Medicare program on a per unit basis.

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.

On January 12, 2025, the HTA Regulation entered into application through a phased implementation. It is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products. The HTA Regulation establishes a framework for joint clinical assessments, joint scientific consultations, and

the early identification of emerging health technologies. The HTA Regulation permits Member States to use common HTA tools, methodologies, and procedures across the European Union and requires them to rely on EU-level joint clinical assessment reports for the clinical components of their national HTA evaluations. EU Member States, however, remain responsible for assessing non-clinical aspects, such as economic, ethical, and social considerations, and for making pricing and reimbursement decisions at the national level. Individual Member States continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. As implementation of the HTA Regulation is phased in and key methodological and procedural guidance continues to evolve, there remains uncertainty regarding the evidence requirements, timing, and impact of joint clinical assessments on national reimbursement processes. The new framework may result in additional or differently structured evidentiary expectations, misalignment between assessment and regulatory timelines, or delays in national decisions. Any adverse or delayed HTA outcomes, or divergent national reimbursement decisions, could negatively affect our ability to obtain or maintain favorable pricing and reimbursement status for any product candidates, if approved. If we are unable to maintain favorable pricing and reimbursement status in Member States for product candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected. In light of the fact that the U.K. has left the EU, the HTA Regulation does not apply in the U.K. However, the U.K. MHRA is working with U.K. HTA bodies and other national organizations, such as the Scottish Medicines Consortium, the National Institute for Health and Care Excellence, and the All-Wales Medicines Strategy Group, to introduce new pathways supporting innovative approaches to the safe, timely and efficient development of medicinal products. There can be no assurance that we will be able to obtain or sustain favorable pricing or reimbursement in the U.K. under these evolving frameworks, and any such inability could materially and adversely affect our anticipated revenues and growth prospects in that market.

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 an 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 U.S. 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 clinical research, proposed sales, marketing and educational programs and other interactions with healthcare professionals. 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. 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;

- the U.S. federal civil and criminal false claims laws, including the FCA, and civil monetary penalty law, 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 civil monetary penalty 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 U.S. 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, or HITECH, 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, and their subcontractors that use disclose or otherwise process individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information;

- the U.S. federal transparency requirements under the 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), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;

- U.S. 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

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

Additionally, we are subject to U.S. 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 payor. 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. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. 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. For further information concerning additional data privacy and security laws we may be subject to and our processing of personal data, see the risk factor titled "*We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our (and the third parties with whom we*

work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenues or profits, and other adverse business consequences."

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 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 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. For example, the ACA, which was signed into law in 2010, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against fraud and abuse, add new transparency requirements for the health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

There have been executive, judicial and Congressional challenges and amendments to certain aspects of ACA. For example, on July 4, 2025, the OBBBA was signed into law, which narrowed access to ACA marketplace exchange enrollment and declined to extend the ACA enhanced advanced premium tax credits that expired at the end of 2025, which, among other provisions in the law, are anticipated to reduce the number of Americans with health insurance. The OBBBA also is expected to reduce Medicaid spending and enrollment by implementing work requirements for some beneficiaries, capping state-directed payments, reducing federal funding, and limiting provider taxes used to fund the program. Congress is considering proposed legislation intended to further reduce healthcare costs with alternatives to replace the expired ACA subsidies. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. Other legislative changes have been approved and adopted since the ACA was enacted, including aggregate reductions to Medicare payments to providers of 2% per fiscal year, which began in 2013, and will remain in effect through 2032 unless additional Congressional action is taken.

The current administration is pursuing policies to reduce regulations and expenditures across government agencies including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. For example, the current administration has announced agreements with several pharmaceutical companies that require the drug manufacturers to offer, through a direct-to-consumer platform, U.S. patients and Medicaid programs prescription drug Most-Favored-Nation pricing equal to or lower than those paid in other developed nations, with additional mandates for direct-to-patient discounts and repatriation of foreign revenues. Other recent actions, for example, include (1) directing agencies to reduce agency workforce and cut programs; (2) directing HHS and other agencies to lower prescription drug costs through a variety of initiatives, including by improving upon the Medicare Drug Price Negotiation Program and establishing Most-Favored-Nation pricing for pharmaceutical products; (3) imposing tariffs on imported pharmaceutical products; and (4) as part of the Make America Healthy Again Commission's Strategy Report released in September 2025, working across government agencies to increase enforcement on direct-to-consumer pharmaceutical advertising. Additionally, the current administration recently called on Congress to enact "The Great Healthcare Plan" to codify and expand Most-Favored-Nation pricing, lower government subsidies to private insurance companies, increase healthcare price transparency, expand pharmaceutical drugs available for over-the-counter purchase, and enact restrictions on pharmacy benefit manager payment methodologies, among other things. These actions and policies may significantly reduce U.S. drug prices, potentially impacting manufacturers' global pricing strategies and profitability, while increasing their operational costs and compliance risks. In addition, the U.S. Supreme Court recently greatly reduced judicial deference to regulatory agencies, which could increase successful legal challenges to federal regulations affecting our operations. Congress may introduce and ultimately pass healthcare-related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program. 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, healthcare reform measures, including 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 healthcare reform and other 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.

We and the third parties with whom we work are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Our (and third parties with whom we work) actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation (including class claims), fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, and other adverse business consequences.

In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive or confidential information, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, and sensitive third-party data (collectively, sensitive information). Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws). For example, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. Numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. To the extent applicable, the exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, referred to collectively as CCPA, applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA allows for fines for noncompliance and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA and other comprehensive U.S. state privacy laws exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and increase compliance costs and potential liability for us and the third parties with whom we work. Similar laws are being considered in several other states, as well as at the federal and local levels, and we expect more states to pass similar laws in the future.

Outside of the United States, an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, the European Union's General Data Protection Regulation, or EU GDPR, and the United Kingdom's GDPR, or U.K. GDPR, impose strict requirements for processing personal data. For example, under the EU GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

We may be subject to new laws governing the privacy of consumer health data, including reproductive, sexual orientation, and gender identity privacy rights. For example, Washington's My Health My Data Act, or MHMD, broadly defines consumer health data, places restrictions on processing consumer health data (including imposing stringent requirements for consents), provides consumers certain rights with respect to their health data, and creates a private right of action to allow individuals to sue for violations of the law. Other states have passed, are considering, and may adopt similar laws.

Our employees and personnel use generative artificial intelligence technologies to perform their work, and the disclosure and use of personal data in generative artificial intelligence technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws and regulations regulating generative artificial intelligence. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative artificial intelligence, it could make our business less efficient and result in competitive disadvantages.

In the ordinary course of business, we transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area, or the EEA, and the U.K., have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and U.K. to the United States in compliance with law, such as the European Commission's Standard Contractual Clauses, the U.K. International Data Transfer Agreement and the U.K. Transfer Addendum, the EU-U.S. Data Privacy Framework and the U.K.'s Extension to that Framework (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the relevant Framework and/or Extension), these mechanisms are subject to potential legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, U.K. or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors, and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and U.K. to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

Additionally, the U.S. Department of Justice issued a rule entitled the Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons, which places additional restriction on certain data transactions involving countries of concern (e.g., China, Russia, Iran) and covered persons (i.e., individuals and entities who are designated as such by the U.S. Attorney General or considered "foreign persons" and are majority-owned by, organized under the laws of, a primary resident in, or a contractor of, a covered person or country of concern, as applicable) that may impact certain business activities such as vendor engagements, sale or sharing of data, employment of certain individuals, and investor agreements. Violations of the rule could lead to significant civil and criminal fines and penalties. The rule applies regardless of whether data is anonymized, key-coded, pseudonymized, de-identified or encrypted, which presents particular challenges for companies like ours and may impact our ability to engage in transactions or agreements with certain third parties in the future.

In addition to data privacy and security laws, we are also bound by other contractual and industry obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful.

We publish privacy policies, marketing materials, whitepapers, and other statements concerning data privacy and security. Regulators in the United States are increasingly scrutinizing these statements, and if these policies, materials, or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading or

misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflicting among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties with whom we work.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties with whom we work may fail to comply with such obligations, which could negatively impact our business operations. Such failures can subject us to potential foreign, local, state and federal action if they are found to be deceptive, unfair, misleading or misrepresentative of our actual practices, which could negatively impact our business operations and compliance posture. If we or the third parties with whom we work fail, or are perceived to have failed, to address or comply with applicable data privacy or security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data; and orders to destroy or not use personal data. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials); inability to process personal data or operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

Our activities 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.

We are subject to laws that regulate certain transactions and access to technology. 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 of 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 Business and Our International Operations

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

As a company with operations in the U.K., 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, including, without limitation, restrictive regulations such as the EU GDPR and U.K. GDPR governing the use, processing, and cross-border transfer of personal data;
- changes in global 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;
- 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.

Any or all of these factors could have a material adverse impact on our business, financial condition and results of operations. Moreover, global instability may continue as a result of geopolitical risks, including evolving impacts from tariffs, sanctions or other trade tensions between the United States and other countries, or demand or supply shocks from events such as major terrorist attacks, war, natural disasters or actual or threatened public health pandemics or other emergencies. These events could have a lasting impact on regional and global economies, any or all of which could disrupt our supply chain and increase the costs associated with or otherwise adversely affect our ability to conduct ongoing and future clinical trials of our product candidates. In addition, continued instability may adversely impact our ability to raise capital in the future on favorable terms or at all.

International trade policies, including tariffs, sanctions and trade barriers may adversely affect our business, financial condition, results of operations and prospects.

The U.S. government has announced substantial new tariffs affecting a wide range of products and jurisdictions and has indicated an intention to continue developing new trade policies, including with respect to the pharmaceutical industry. In response, certain foreign governments have announced or implemented retaliatory tariffs and other protectionist measures. These developments have created a dynamic and unpredictable trade landscape, which may adversely affect our business, results of operations, financial conditions and prospects. For example, in February 2026, the United States Supreme Court (SCOTUS) invalidated certain tariffs imposed by the U.S. government under emergency statutory authority in 2025. Shortly thereafter, President Trump signed an executive order implementing a new 10% global tariff pursuant to an alternative statutory authority, which may be raised up to 15%. It remains unclear whether and to what extent duties previously collected under the invalidated tariffs will be refunded, whether refunds will be subject to administrative or judicial processes, or whether offsets or alternative measures may be imposed. In addition, the Bureau of Industry and Security, U.S. Department of Commerce, has initiated an investigation to determine whether pharmaceutical ingredients, including finished drug product, manufactured outside the United States pose a national security risk and should be subject to additional tariffs.

We do not own or operate any manufacturing facilities for production of clinical or commercial supply. We currently rely, and expect to continue to rely on third parties, including those located in China, for supply of our product candidates, as well as for manufacture of any products that we may commercialize, if approved. For further information concerning our reliance on third parties, see the risk factor titled "*Risks Related to Our Dependence on Third Parties—We intend to rely on third parties to manufacture product candidates and supply raw materials used in our product candidates, such as ^{212}Pb, 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.*"

Current or future tariffs or other trade barriers may result in increased research and development expenses, including with respect to increased costs associated with active pharmaceutical ingredients, raw materials, laboratory equipment and research materials and components. In addition, such tariffs may increase our supply chain complexity and could also potentially disrupt our existing supply chain. Unlike consumer goods, pharmaceuticals face unique regulatory constraints that make rapid supply chain adjustments particularly difficult and costly. Trade restrictions

affecting the import of materials necessary for clinical trials could result in delays to our development timelines. Increased development costs and extended development timelines could place us at a competitive disadvantage compared to companies operating in regions with more favorable trade relationships and could reduce investor confidence, negatively impacting our ability to secure additional financing on favorable terms or at all. In addition, as we advance toward commercialization in the future, tariffs and trade restrictions could hinder our ability to establish cost-effective production capabilities, negatively impacting our growth prospects.

The complexity of announced or future tariffs may also increase the risk that we or our customers or suppliers may be subject to civil or criminal enforcement actions in the United States or foreign jurisdictions related to compliance with trade regulations. Foreign governments may also adopt non-tariff measures, such as procurement preferences or informal disincentives to engage with, purchase from or invest in U.S. entities, which may limit our ability to compete internationally and attract non-U.S. investment, employees, customers and suppliers. Foreign governments may also take other retaliatory actions against U.S. entities, such as decreased intellectual property protection, increased enforcement actions, or delays in regulatory approvals, which may result in heightened international legal and operational risks. In addition, the United States and other governments have imposed and may continue to impose additional sanctions, such as trade restrictions or trade barriers, which could restrict us from doing business directly or indirectly in or with certain countries or parties and may impose additional costs and complexity to our business.

Cyber-attacks, failures in or interruptions of, or other compromise to our information technology systems, or those of third parties with whom we work, or our data could result in adverse consequences that materially affect our business, including without limitation, regulatory investigations or actions, litigation, fines and penalties, information theft, data corruption, harm to our reputation and brand, significant disruption of our business operations, and other adverse consequences.

In the ordinary course of business, we and the third parties with whom we work process sensitive information. Cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties with whom we work. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors.

Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties with whom we work may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability conduct our research and development programs and our clinical trials. We and the third parties with whom we work may be subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks and deep fakes, which may be increasingly more difficult to identify as fake), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing attacks, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, attacks enhanced or facilitated by artificial intelligence, or AI, and other similar threats. In particular, severe ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, disruption of clinical trials, loss of sensitive data (including data related to clinical trials), loss of income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Remote work has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers, and devices outside of our premises or network, including working at home, while in transit and in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found

during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

In addition, our reliance on third-party service providers could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We rely on third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, third-party providers of information technology infrastructure, cloud-based infrastructure, encryption and authentication technology, employee email, content delivery to customers, CROs for managing clinical trial data, and other functions. We also rely on third-party service providers to provide other products, services, parts, or otherwise operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, the liability of such third party may be limited such that any award may be insufficient to cover our damages, or we may be unable to recover any such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

We may expend significant resources or modify certain of our business activities (which could include our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures, industry-standard or reasonable security measures to protect our information technology systems and sensitive information.

While we have established physical, electronic and organizational security measures designed to safeguard and secure our systems against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate and remediate vulnerabilities in our information technology systems (such as our hardware and/or software, including that of third parties with whom we work). We may not, however, detect and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties with whom we work. For example, we have been the target of unsuccessful phishing attempts in the past and we expect such attempts will continue in the future. A security incident or other interruption could disrupt our ability (and that of third parties with whom we work) to provide our products or services. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Applicable data privacy and security obligations may require us, or we may voluntarily choose, to notify relevant stakeholders, including affected individuals, customers, regulators and investors, of security incidents, or to take other actions, such as providing credit monitoring and identity theft protection services. Such disclosures and related actions can be costly, and the disclosure or the failure to comply with such applicable requirements could lead to adverse consequences. If we (or a third party with whom we work) experience a security incident or are perceived to have experienced a security incident, we may experience material adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class-action claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant material consequences may cause customers to stop using our services, deter new customers from using our services, and negatively impact our ability to grow and operate our business. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security

obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

Additionally, our sensitive information, including personal data, could be leaked, disclosed or revealed as a result of, or in connection with, our employees', personnel's, or vendors' use of generative artificial intelligence technologies.

Social media platforms and artificial intelligence-based platforms present new risks and challenges to our business.

Social media is increasingly being used to communicate information about us, our programs and the diseases our therapeutics are being developed to treat. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations or other consequences. Further, the accidental or intentional disclosure of non-public information by our workforce or others through media channels could lead to information loss. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us, our products, or our product candidates on any social media platform. The nature of social media prevents us from having real-time control over postings about us on social media. We may not be able to reverse damage to our reputation from negative publicity or adverse information posted on social media platforms or similar mediums. If any of these events were to occur or we otherwise fail to comply with application regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business including quick and irreversible damage to our reputation, brand image and goodwill.

Additionally, AI-based platforms are increasingly being used in the pharmaceutical industry and we are expanding the use of AI-based platforms in our operations for data analysis, summarization and automation, which subjects us to a variety of risks, including potential cybersecurity vulnerabilities, breaches of data privacy and the potential for inadvertent or unauthorized disclosure of our confidential information and intellectual property. Our use, or the use by our vendors, suppliers and contractors with access to our proprietary and confidential information, including trade secrets, may lead to the release of our proprietary and confidential information, which may negatively impact our company, including our ability to realize the benefit of our intellectual property. Moreover, AI-based platforms may create flawed, incomplete, or inaccurate outputs, some of which may appear correct. This may happen if the inputs that the model relied on were inaccurate, incomplete or flawed (including if a bad actor "poisons" the AI-based platform with bad inputs or logic), or if the logic of the AI-based platform is flawed (a so-called "hallucination").

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 U.K., we source research and development, manufacturing, consulting and other services from the United States, 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. Any fluctuation in the exchange rate of these foreign currencies may negatively impact our business, financial condition and operating results. Global economic events have and may continue to significantly impact local economies and the foreign exchange markets, which may increase the risks associated with sales denominated in foreign currencies.

Risks Related to Our Dependence on Third Parties

For certain product candidates, we depend, or may depend, on development and commercialization collaboration partners to develop, conduct clinical trials, obtain regulatory approvals of, and if approved, market and sell product candidates. If such partnerships 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 may depend, on development and commercialization collaboration partners to develop, conduct clinical trials of, and, if approved, sell product candidates.

Under our existing collaborations with Ionis and Bayer, 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. 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.

From time to time, we may also explore partnership opportunities for certain of our product candidates, such as BT7480. However there can be no assurance that we will be able to do so, or that such relationships, if established, will be successful or on favorable terms.

Our current collaborations and any future collaborations or partnerships 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;

- adverse global economic events, including public health crises, could materially affect our operations as well as causing significant disruption in the operations and business of our collaborators and the third-party manufacturers, CROs and other service providers that we and/or our collaborators conduct business with; 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 were previously involved in 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.

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. 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.

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. 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 Bicycle molecules may have utility, we intend to continue to rely on external service providers.

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 EEA countries 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 any of the third parties conducting clinical trials on our behalf, including clinical investigators, do not successfully carry out their contractual duties for any reason, 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, manufacturing issues, 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 and supply raw materials used in our product candidates, such as ^{212}Pb, 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, including those located in China, for supply of our product candidates, and our strategy is to outsource all manufacturing of our product candidates and products to third parties. For any activities conducted in China, we are exposed to the increased possibility of supply disruptions and higher costs in the event of changes in the policies of the U.S. or Chinese governments including tariffs, political unrest or unstable economic conditions including sanctions on China or any of our China-based suppliers. Our manufacturing costs could also increase as a result of future appreciation of the local currency in China or increased labor costs if the demand for skilled laborers increases and/or the availability of skilled labor declines in China. In addition, certain Chinese biotechnology companies may become subject to trade restrictions, sanctions, other regulatory requirements, or proposed legislation by the U.S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting the supply of material to us. Such disruption could have adverse effects on the development of our product candidates and our business operations. For example, the United States has recently passed legislation, namely the BIOSECURE Act, to prohibit U.S. federal executive agencies from procuring or obtaining any biotechnology equipment or service produced or provided by a "biotechnology company of concern," or BCC, or entering into or renewing a contract, loan, or grant with an entity that uses such biotechnology equipment or service. Specifically, on December 18, 2025, President Trump signed the National Defense Authorization Act for fiscal year 2026 into law, which includes the BIOSECURE Act. The BIOSECURE Act prohibits the U.S. government from procuring or obtaining biotechnology equipment or services produced or provided by a BCC; entering into, extending, or renewing government contracts with an entity that directly or indirectly uses biotechnology equipment or services from a BCC in performance of that federal contract; and/or issuing grants or loans to purchase, obtain, or use biotechnology equipment or services produced by a BCC. The BIOSECURE Act also prohibits U.S. government loan and grant recipients from using federal loan or grant money to enter into contracts with entities that use equipment from BCCs in the performance of any federal prime contract or subcontract. Companies designated as a BCC include those that are identified on the U.S. Department of Defense's annual List of Chinese Military Companies, also known as the 1260H List, and the U.S. government also has the ability to designate entities as BCCs through a separate designation process. There is a "safe harbor" provision providing that the restrictions do not apply to equipment or services that were formerly but are no longer provided by a BCC, as well as a "grandfathering" provision providing that the prohibitions shall not apply for a five-year period to biotechnology equipment or services produced or provided under a contract or

agreement entered into before the applicable effective date. Given the BIOSECURE Act, we may be restricted in our ability to work with certain Chinese biotechnology companies to the extent we would contract with, or otherwise receive funding from, the U.S. government.

We are substantially dependent on third parties for supply of our raw material used in our product candidates. Although we believe our present suppliers have adequate quantities of raw material to meet our current needs, we may encounter supply shortages which could adversely affect our business. There can be no assurance that our suppliers will renew contracts on acceptable terms, or at all. In addition, as it relates to our BRC and BIA molecules, we expect future product candidates to include ^{212}Pb or other radioisotopes. While we have announced arrangements with the United Kingdom Nuclear Decommissioning Authority, United Kingdom National Nuclear Laboratory and SpectronRx for the ultimate supply of ^{212}Pb and Eckert & Ziegler for a range of radioisotopes, there are not many alternatives to these suppliers, and finding any replacement suppliers would divert management resources.

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. Additionally, our manufacturers may experience delays as a result of impacts due to geopolitical risks, including evolving impacts from tariffs, sanctions or other trade tensions between the United States and other countries, or demand or supply shocks from events such as major terrorist attacks, war, natural disasters or actual or threatened public health pandemics or other emergencies. For example, the United States has announced tariffs on many goods imported from specified nations, including China and those in the European Union. In addition, there are currently discussions concerning potential increased tariffs for pharmaceutical products, which may impact our supply chain and create uncertainty in the broader pharmaceutical industry. While certain tariffs have been suspended, modified or temporarily reduced, we cannot predict the results of the U.S. government's trade negotiations or the outcome of ongoing legal challenges to specific tariff policies. If our 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 cGMP 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 nuzefatide pevedotin, 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, including as a result of the impacts of public health crises on the global workforce and manufacturing operations, 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.

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 United States Patent and Trademark Office (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. As an example of the foregoing risks, the validity of our European Patent No. 4464721 has been challenged by an opponent at the European Patent Office. Proceedings are ongoing, during which the patent may be maintained, narrowed or invalidated. 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 may materially harm our intellectual property estate, 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 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.

The patent positions of companies in development and commercialization of biologics and pharmaceuticals are uncertain. Changes in either the patent laws or the interpretation of the patent laws in the United States or other jurisdictions could further increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For example, 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.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we were previously party to protracted litigation with Pepscan, which we settled in 2020. We may become party to, or be 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

on 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 have been in the past and may be subject in the future 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. 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 invalid, 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 objections. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such objections.

In addition, in the USPTO and in comparable Intellectual Property Offices 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 have been and may in the future be filed against our trademarks, and our trademarks may not survive such proceedings. For example, our U.K. trademark application for "TICA" was successfully opposed in the U.K., Japan and the EU for the majority of goods and services for which we originally applied, and we have abandoned our trademark application for "TICA" in the United States as a result. 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

Our recent workforce reductions were undertaken to significantly reduce our ongoing operating expenses, but they may not result in our intended outcomes and may yield unintended consequences and additional costs.

In August 2025, we announced cost reduction initiatives that are expected to reduce planned operating costs, primarily through a workforce reduction. This workforce reduction was substantially completed in the fourth quarter of 2025. As a result, we incurred aggregate charges, representing cash expenditure for severance and other employee termination benefits, of approximately $5.3 million during the year ended December 31, 2025.

In addition, in conjunction with our strategic reprioritization announced in March 2026, we are implementing a proposed workforce reduction of approximately 30% of our workforce. Together, the workforce reduction and strategic reprioritization are expected to reduce our annual operating expenses by approximately 50% based on our current plans. We expect this workforce reduction to be substantially completed by the end of 2026, and that we will incur aggregate charges, representing cash expenditure for severance and other employee termination benefits, of approximately $8.0 million.

These recent workforce reductions may result in unintended consequences and costs, such as the loss of institutional knowledge and expertise, attrition beyond the intended number of employees, decreased morale among our remaining employees, and the risk that we may not achieve the anticipated benefits of the workforce reductions. In addition, we may be unsuccessful in distributing the duties and obligations of departed employees among our remaining employees or to contractors or other partners. The workforce reductions could also make it difficult for us to pursue, or prevent us from pursuing, new opportunities and initiatives due to insufficient personnel, or require us to incur additional and unanticipated costs to hire new personnel to pursue such opportunities or initiatives. Further, inflationary pressure may increase our costs, including employee compensation costs, or result in employee attrition to the extent our compensation does not keep up with inflation, particularly if our competitors' compensation does. If we are unable to realize the anticipated benefits from the workforce reductions, if we experience significant adverse consequences from the workforce reductions, or if we are otherwise unable to retain our employees, our business, financial condition, and results of operations may be materially adversely affected.

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 key 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 and personnel 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.

Particularly in light of our recent workforce reductions, we may find it difficult to maintain valuable aspects of our culture, to prevent a negative effect on employee morale or attrition beyond our planned reduction in headcount, and to attract and retain competent personnel. If we are not able to continue to retain, on acceptable terms, the qualified personnel necessary for the continued operation of our business, we may not be able to sustain our operations. 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 CROs 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. Further, because of our hybrid work environment, information that is normally protected, including company confidential information, may be less secure. We have adopted a code of conduct and business ethics to which all of our employees must adhere, 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 may encounter difficulties in managing our growth, which could disrupt our operations.

In recent years, we have experienced significant fluctuations in the number of our employees and growth in the scope of our operations and over the long term we expect to expand, particularly in the areas of drug manufacturing, supply chain, clinical development, sales, marketing, 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 time and attention to managing both rightsizing and growth activities.

Our potential growth over the long term may also 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 Massachusetts, U.S. Due to our limited resources, we may not be able to effectively manage the potential expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to effectively manage changes in the size of our workforce and other 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 potential 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 potential 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 IPO in May 2019, through March 12, 2026, the trading price of our ADSs has ranged from $5.04 to $62.08. The stock market in general, and the market for pharmaceutical 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 the 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 partners 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.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, supply chain shortages, increases in inflation rates, higher interest rates and uncertainty about economic stability. Similarly, geopolitical risks, including evolving impacts from tariffs, sanctions or other trade tensions between the United States and other countries, or demand or supply shocks from events such as major terrorist attacks, war, natural disasters or actual or threatened public health pandemics or other emergencies have created extreme volatility in the global capital markets and may have further global economic consequences, including further disruptions of the global supply chain and energy markets. Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely. If the equity and credit markets continue to deteriorate, it may make any necessary debt or equity financings more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. Increased inflation rates and macroeconomic turmoil can adversely affect us by increasing our costs and the costs of our contract manufacturing organizations, or CMOs, and other suppliers. These factors may negatively affect the market price of our ADSs, regardless of our actual operating performance.

The dual class structure of our shares may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

As of March 12, 2026, we had 50,269,082 ordinary shares, nominal value £0.01 per share, and 19,437,944 non-voting ordinary shares, nominal value £0.01 per share, outstanding. The dual class structure of our shares may limit your ability to influence corporate matters. Holders of our ordinary shares are entitled to one vote per share, while holders of our non-voting ordinary shares are not entitled to any votes. Nevertheless, non-voting ordinary shares may be re-designated at any time as ordinary shares at the option of the holder by providing written notice to us, subject to certain

restrictions. Such restrictions include prohibitions on a holder from re-designating the non-voting ordinary shares as ordinary shares if such re-designation would result in such holder beneficially owning (when aggregated with "affiliates" and "group" members) in excess of 9.99% of any class of our securities registered under the Exchange Act, or upon at least 61 days' notice, not in excess of 19.9%. Any re-designation of non-voting ordinary shares as ordinary shares will have the effect of increasing the relative voting power of those prior holders of our non-voting ordinary shares, and correspondingly decreasing the voting power of the holders of our ordinary shares, which may limit your ability to influence corporate matters. The ordinary shares currently have 100% of the voting power, but if the holders of non-voting ordinary shares were to re-designate all of their non-voting ordinary shares as ordinary shares (assuming, for these purposes, that they were able to do so in compliance with the beneficial ownership limitation), based on the number of ordinary shares and non-voting ordinary shares outstanding on December 31, 2025, the ordinary shares outstanding prior to the re-designation would have approximately 72% of the voting power and the former non-voting ordinary shares would represent approximately 28% of the voting power.

Substantial future sales or issuances of shares of our ordinary shares or ADSs or other equity-related securities could adversely affect the price of our ADSs and dilute shareholders.

Sales of a substantial number of ordinary shares or ADSs, and sales by our management, our directors, their affiliates, or significant shareholders, could occur at any time. Based on information available to us, entities affiliated with Baker Bros. Advisors LP, or the Baker Entities, beneficially own approximately 21.7% of our ordinary shares. If these shares are sold in the market in transactions that occur at about the same time, such transactions could depress the market of our ADSs and could also affect our ability to raise equity capital through the sale of additional equity or equity-related securities, including non-voting ordinary shares, to meet our capital needs, including in connection with funding potential future acquisition or licensing opportunities, capital expenditures or product development costs. Our registration obligations pursuant to the Registration Rights Agreement with the Baker Entities also cover all shares thereafter acquired by the Baker Entities, for up to 10 years, and include our obligation to facilitate certain underwritten public offerings of our ordinary shares or ADSs by the Baker Entities in the future. 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, which will dilute current holders.

Our existing shareholders may consult with our management and have various impacts on our business affairs.

While our shareholder base and relative holdings may change over time, the Baker Entities hold the largest ownership position in our outstanding ordinary shares and non-voting ordinary shares. In addition, Felix J. Baker, Chairman of our board of directors, is a managing member of Baker Bros. Advisors (GP) LLC, which is the sole general partner of Baker Bros. Advisors LP. The interests of the Baker Entities and its affiliates may not always coincide with the interests of other shareholders, and any influence exerted over our business and affairs by these entities may not coincide with the wishes of other shareholders.

In addition, our executive officers and directors and holders of greater than five percent of our outstanding ordinary shares beneficially owned approximately 47% of our voting power as of March 12, 2026. As a result, these shareholders in aggregate are able to exert substantial influence over our management and affairs and matters requiring shareholder approval, including the election of directors and approval of significant corporate transactions, such as mergers, consolidations or the sale of substantially all of our assets. Consequently, this concentration of ownership may result in our taking corporate actions that our other shareholders may not consider to be in their best interest. For example, it may have the effect of delaying, deferring or preventing a change in control, including a merger, consolidation, takeover or other business combination involving us or discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control, which might affect the market price of our ADSs.

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.

Risks Related to Our Incorporation Under the Laws of England and Wales

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 U.K. 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 U.K. In addition, uncertainty exists as to whether U.K. courts would entertain original actions brought in the U.K. 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 U.K. 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.

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, including cash. 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 United States person holds our shares, such U.S. shareholder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred and additional reporting requirements.

Based on our analysis of our income, assets, activities and market capitalization, we believe that we were a PFIC in the 2025 taxable year. In addition, no assurances can be provided that we will not be a PFIC for any future taxable year or that we have not been a PFIC in any prior taxable years. 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. In the event we are a PFIC, we intend to provide the information necessary for U.S. holders to make a qualified electing fund election.

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 U.K., we are subject to U.K. corporate taxation. 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 the Corporate Income Loss Restriction and the Corporate Capital Loss Restriction that, broadly, restrict the amount of carried forward losses that can be utilized to 50% of group profits or gains arising above £5.0 million per tax year), we expect losses to be eligible for carry forward and utilization against future operating profits. In addition, if we were to have a major change in the nature of the conduct or the conduct of our trade, loss carryforwards may be restricted or extinguished.

As a group that carries out extensive research and development, or R&D, activities, we seek to benefit from the U.K. R&D tax credit regime. In respect of accounting periods in which we qualify as a Small and Medium-sized Enterprise, or SME, and in which our relevant R&D expenditure represents 30% or more of the total relevant expenditure (meaning we also qualify as "R&D intensive" during such accounting period), we may, under this regime, surrender the trading losses that arise from our R&D activities for a cash rebate of up to 26.97% of qualifying R&D expenditure. Accordingly, if we cease to qualify as an R&D-intensive SME in the future, we will either cease to be able to claim cash rebates in respect of our R&D activities, or only be able to receive cash payments or other tax relief (under other provisions of the U.K. R&D tax credit regime) at a significantly lower rate than at present. Further, the regime's rules are complex, and if a tax authority were to challenge or seek to disallow our claims (in whole or in part), for example by asserting that we do not (or the relevant expenditure does not) meet the technical conditions to be granted tax credits (or cash rebates), then such challenge or disallowance, if successful, could have a material impact on our cash-flow and financial performance. In addition, future changes to the U.K. R&D tax credit regime may mean that we no longer qualify for it or have a material impact on the extent to which we can make claims (or benefit from them).

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% by giving an additional tax deduction. 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 eligible for this tax deduction. When taken in combination with the enhanced relief available on our R&D expenditures, we expect a long-term rate of corporation tax lower than the statutory rate to apply to us. If, however, there are unexpected adverse changes to the U.K. R&D tax relief programs 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. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

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, and our ADSs and ordinary shares are, subject to changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration or being implemented by tax authorities in jurisdictions in which we operate, including in connection with tax policy initiatives and reforms led by the Organization for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit

Shifting, or BEPS, Project (including "BEPS 2.0") and the European Commission. 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, or the stamp duty or stamp duty reserve tax treatment of our ADSs or ordinary shares.

The IRA includes a minimum tax equal to 15% of the adjusted financial statement income of certain corporations, as well as a 1% excise tax on share buybacks. In addition, the OBBBA includes provisions affecting corporate tax rates on specified eligible income, timing of tax deductibility of depreciation, interest expense and research and development costs, and the taxation of foreign income. For example, for tax years beginning after December 31, 2024, the OBBBA restores the tax deductibility of domestic research and development expenses in the year incurred, which expenses had been required under prior legislation to be capitalized and subsequently amortized over five years. The OBBBA did not change the tax treatment of expenses incurred in research and development activities conducted outside the United States, which expenses continue to be required to be capitalized and amortized over 15 years. Future guidance from the Internal Revenue Service and other tax authorities with respect to any legislation may affect us, and certain aspects of such legislation could be repealed or modified in future legislation or sunset in future years. 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, or may apply existing rules in an unforeseen manner, 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. 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.

Under transitional provisions that apply until February 2, 2027, the U.K. City Code on Takeovers and Mergers, or the Takeover Code, can apply to an offer for, among other things, a public company whose registered office is in the United Kingdom (but is not listed 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 before the end of the transitional period 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.

Following the end of the transitional period, with effect from February 3, 2027, the "residency test" will be abolished in its entirety and we expect we will no longer be subject to the jurisdiction of the Takeover Code at all from that time, unless our securities are listed 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, the number of shares determines the number of votes a holder may cast only on a poll. However, 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; and

- 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.

General Risks

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. Our management is required to assess the effectiveness of our controls over financial reporting annually. Pursuant to Section 404, we are also 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. 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 consolidated 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 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.

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.

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.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

Not Applicable.

ITEM 1C. CYBERSECURITY.

Risk management and strategy

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our critical computer networks, third-party hosted services, communications systems, computer hardware and software, and our critical data, which includes proprietary, confidential and sensitive data, including, without limitation, personal data (such as health-related data), intellectual property and trade secrets, referred to collectively as Information Assets. Accordingly, we maintain certain risk assessment processes intended to identify cybersecurity threats, determine their likelihood of occurring, and assess potential material impact to our business. Based on our assessment, we implement and maintain risk management processes designed to protect the confidentiality, integrity, and availability of our Information Assets and mitigate harm to our business.

Risks from cybersecurity threats are among those that we address in our general risk management program. We rely on a multidisciplinary team (including personnel from our information security function, management and third-party service providers, as needed, as described further below) to help identify, assess and manage our risks. We identify and assess such threats by, among other things, monitoring and evaluating the threat environment using various methods, including, for example, manual and automated tools, information security tools and platforms to alert us to potentially unwarranted activity on our networks, subscribing to reports and services that identify cybersecurity threats, analyzing reports of threats and actors, conducting scans of the threat environment, evaluating our and our industry's risk profile, evaluating threats reported to us, conducting threat assessments for internal and external threats, and conducting risk and vulnerability assessments to identify vulnerabilities.

Depending on the environment, we implement and maintain various technical, physical and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Assets. For example, the risk management and reduction measures we implement for certain of our Information Assets include: policies and procedures designed to address cybersecurity threats, including an incident response plan, vulnerability management, and disaster recovery/business continuity plans; incident detection and response solutions; internal and/or external audits to assess our exposure to cybersecurity threats; documented risk assessments; implementation of certain security standards/certifications; encryption of data; network security controls; data segregation; physical and electronic access controls; physical security; asset management, tracking and disposal; systems monitoring; employee security training; penetration testing; and cyber insurance. In addition to the above, management obtains a third-party review and formal certification of its information management system policies and procedures, which has been collated into an Information Security Management System (ISMS) which is maintained to ISO27001 standards.

We work with third parties from time to time that assist us to identify, assess, and manage cybersecurity risks, including professional services firms, threat intelligence service providers, cybersecurity consultants, cybersecurity software providers, managed cybersecurity service providers, penetration testing firms and other vendors that help to identify, assess, or manage cybersecurity risks.

To operate our business, we utilize certain third-party service providers to perform a variety of functions, such as outsourced business critical functions including contract research organizations, or CROs, for managing clinical trials, professional services, SaaS platforms, managed services, property management, cloud-based infrastructure, data center facilities, content delivery to customers, encryption and authentication technology, corporate productivity services, and other functions. We generally engage reliable, reputable service providers that maintain cybersecurity programs. Depending on the nature of the services provided, the sensitivity and quantity of information processed, and the identity of the service provider, our vendor management process may include reviewing the cybersecurity practices of such provider, contractually imposing obligations on the provider related to the services they provide and/or the information they process, conducting security assessments, requiring their completion of written questionnaires regarding their services and data handling practices, and conducting periodic re-assessments during their engagement.

For service providers that provide particularly critical services to us or process particularly sensitive information for us, we may also require that such providers possess at least one of the following certificates, reports, or procedures: SOC 2 Type 2; ISO 27001; annual penetration tests; and/or red/blue team tests.

For a description of the risks from cybersecurity threats that may materially affect us and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including the risk factor titled: *Cyber-attacks, failures in or interruptions of, or other compromise of our information technology systems, or those of third parties with whom we work, or our data could result in adverse consequences that materially affect our business, including without limitation, regulatory investigations or actions, litigation, fines and penalties, information theft, data corruption, harm to our reputation and brand, significant disruption of our business operations and other adverse consequences*.

Governance

Our cybersecurity risk management strategy relies on input from management, including our Vice President, Information Technology & Cybersecurity, who reports directly to our Chief Operating Officer, and has over a decade of experience in developing and implementing cybersecurity strategies for companies in the biopharmaceutical industry, as well as our Chief Financial Officer and Chief Legal Officer and General Counsel. We also operate an Information Risk Operating Committee, or IROC, consisting of senior members of the finance, legal, operations and information technology functions, to oversee the management of information security as a whole, including integrating cybersecurity considerations into the company's overall risk management strategy, and for communicating key priorities to employees. The IROC meets on a regular basis, generally quarterly, to discuss cybersecurity risk and to review our cybersecurity program.

Our cybersecurity incident response and vulnerability management processes are designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including our incident response team, which includes, but is not limited to, our Vice President, Information Technology & Cybersecurity, Chief Legal Officer and General Counsel and Chief Financial Officer. In addition, our incident response processes include reporting to the Audit Committee of the board of directors for certain cybersecurity incidents.

Management, including the IROC, is also responsible for approving budgets, helping prepare for cybersecurity incidents, responding to cybersecurity incidents, approving cybersecurity policies and procedures, reviewing audit reports, and reporting to the board of directors.

Our board of directors oversees our risk management strategy with respect to cybersecurity threats. The board, through its Audit Committee, holds regular meetings, at least quarterly, to discuss issues including our cybersecurity threats. The meetings involve presentations and reports from our management, including our Vice President, Information Technology & Cybersecurity, concerning our significant cybersecurity threats and risks and the processes we have implemented to address them.

ITEM 2. PROPERTIES.

We occupy approximately 45,000 rentable square feet of office and laboratory space in Cambridge, United Kingdom under a lease that expires in December 2031, and may be renewed for 10 years, cancelable in the fifth year of the extension. We also lease an additional 11,000 rentable square feet of office and laboratory space in Lexington, Massachusetts under a lease that expires in December 2027 and approximately 23,000 rentable square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in March 2026. 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. We are not currently subject to any material legal proceedings.

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

Neither our ordinary shares, nominal value £0.01 per share, nor our non-voting ordinary shares, nominal value £0.01 per share, are 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, ordinary shares, or non-voting ordinary shares.

Holders of Ordinary Shares

As of March 12, 2026, there were approximately 45 holders of record of our ordinary shares, two holders of record of our non-voting 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

Not Applicable.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. [Reserved]

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, or this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, 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, 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, 2024 compared to the year ended December 31, 2023, 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 Company's Annual Report on Form 10-K for the year ended December 31, 2024, which was filed with the Securities and Exchange Commission, or the SEC, on February 25, 2025.

Overview

We are a clinical-stage pharmaceutical company developing a novel class of medicines, which we refer to as Bicycle® molecules, for diseases that are underserved by existing therapeutics. Bicycle molecules are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making Bicycle molecules attractive candidates for drug development. Bicycle molecules 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 Bicycle molecules allows targets to be drugged that have historically been intractable to non-biological approaches. Bicycle molecules are excreted by the kidney rather than the liver and have shown no significant signs of immunogenicity to date, qualities which we believe explain the molecules' favorable toxicological profile.

We have a novel and proprietary phage display screening platform which we use to identify Bicycle molecules 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 quintillions of potential Bicycle molecules 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 internal programs are focused on oncology indications with high unmet medical need. Our product candidate, nuzefatide pevedotin, formerly BT5528, is a Bicycle Drug Conjugate, or a BDC® molecule, whereby the Bicycle molecules are chemically attached to a toxin that, when administered, is cleaved from the Bicycle molecule and kills the tumor cells. We are evaluating nuzefatide pevedotin, a BDC molecule targeting Ephrin type A receptor 2, or EphA2, in both an ongoing company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and clinical activity in patients with advanced solid tumors and an ongoing company-sponsored Phase II clinical trial to evaluate the efficacy, safety and pharmacokinetics of nuzefatide pevedotin in adult patients with recurrent metastatic pancreatic ductal adenocarcinoma after progression on a first-line therapy, which commenced recruiting patients in the first quarter of 2026. We are also developing BT1702, a Bicycle Radioconjugate, or BRC®, molecule targeting Membrane Type 1 matrix metalloproteinase, or MT1-MMP, and carrying a lead-212, or ^{212}Pb, radioisotope payload for theranostic use. We are currently conducting Investigational New Drug application, or IND, -enabling activities for BT1702. We are also developing Bicycle Imaging Agents, or BIA molecules. In a BIA molecule a Bicycle molecule is linked to a chelated radiopharmaceutical imaging agent. We are using BIA molecules to potentially derisk novel targets prior to further clinical development and to efficiently triage cancer indications for subsequent treatment with both BRC and BDC molecules. Our discovery pipeline in oncology includes next-generation BDC molecules, BRC molecules and BIA molecules.

Zelenectide pevedotin, a BDC molecule targeting Nectin-4, is being evaluated in an ongoing company-sponsored Phase I/II clinical trial to assess the safety, pharmacokinetics and clinical activity in patients with Nectin-4 expressing advanced malignancies, an ongoing Phase II/III registrational trial called Duravelo-2 evaluating zelenectide pevedotin in patients with untreated and previously treated metastatic urothelial cancer and in ongoing company-sponsored Phase I/II clinical trials to assess the efficacy and safety of zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer, which commenced recruiting patients in the first and third quarters of 2025, respectively. In March 2026, we announced the strategic reprioritization of our clinical portfolio to focus on our promising pipeline of next-generation therapeutics, including nuzefatide pevedotin as well as next-generation Bicycle conjugates, including BRC molecules. While dose selection data from the clinical trial for zelenectide pevedotin are promising, demonstrating response rates comparable to published rates for existing standards of care and a differentiated safety profile, we plan to convert the Phase II/III Duravelo-2 registrational trial to a randomized Phase II clinical trial and deprioritize the program for internal development while we evaluate next steps for zelenectide pevedotin following preliminary feedback from regulatory agencies. In addition, as part of the strategic reprioritization, we plan to discontinue the Phase I/II clinical trials evaluating zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer. Further enrollment in these trials will be closed and patients already enrolled will complete their course of treatment.

Our other product candidate, BT7480, is a Bicycle Tumor-Targeted Immune Cell Agonist®, or Bicycle TICA® molecule. A Bicycle TICA molecule links immune cell receptor binding Bicycle molecules to tumor antigen binding Bicycle molecules. BT7480, a Bicycle TICA molecule targeting Nectin-4 and agonizing CD137, is being evaluated in a company-sponsored Phase I/II clinical trial. After reporting certain data from the clinical trial in the first half of 2026, we will no longer develop BT7480 internally and intend to explore partnership opportunities for future development.

Beyond our wholly owned oncology portfolio, we are collaborating with biopharmaceutical companies and organizations in additional therapeutic areas in which we believe our proprietary Bicycle screening platform can identify therapies to treat diseases with significant unmet medical need.

Workforce Reductions

In August 2025, we announced cost reduction initiatives to reduce planned operating costs, primarily through a workforce reduction that was substantially complete as of December 31, 2025. As a result, we incurred aggregate charges for severance and other employee termination benefits of $5.3 million during the year ended December 31, 2025. In addition, in March 2026, we announced the strategic reprioritization of our clinical portfolio to focus on our promising pipeline of next-generation therapeutics, including nuzefatide pevedotin as well as next-generation Bicycle conjugates, including BRC molecules. In connection with the strategic reprioritization, we are implementing a proposed workforce reduction of approximately 30% of our workforce. Together, the workforce reduction and strategic reprioritization are expected to reduce our annual operating expenses by approximately 50% based on our current plans. We expect the workforce reduction to be substantially completed by the end of 2026, and that we will incur aggregate charges, representing cash expenditure for severance and other employee termination benefits, of approximately $8.0 million.

Financial Overview

Since our inception, we have devoted substantially all of our resources to developing our Bicycle platform and our product candidates, 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 our equity securities; proceeds received from upfront payments, research and development payments, and development milestone payments from our collaboration agreements; and borrowings pursuant to a loan and security agreement, or the Loan Agreement, with Hercules Capital, Inc., or Hercules. From our inception in 2009 through December 31, 2025, we have received gross proceeds of $1.4 billion from the sale of equity securities and $239.6 million of cash payments under our collaboration agreements, including $46.3 million

from Bayer Consumer Care AG, or Bayer, $53.0 million from Novartis Pharma AG, or Novartis, $49.7 million from Ionis Pharmaceuticals, Inc., or Ionis, and $56.0 million from Genentech Inc., or Genentech. 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 $219.0 million, $169.0 million and $180.7 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $899.8 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 expect that our expenses and capital requirements will decrease in the near term as a result of our cost saving initiatives and our strategic reprioritization announced in March 2026. However, our expenses and capital requirements may increase substantially if and as we:

- continue our development of our product candidates, including conducting future clinical trials of nuzefatide pevedotin and BT1702;
- seek to identify and develop additional product candidates, including expanding our pipeline of Bicycle radioligand molecules and next-generation BDC molecules;
- 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 and any future commercialization efforts.

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 encouraging 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

and governmental 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, 2025, we had cash and cash equivalents of $628.1 million. We believe that our existing cash and cash equivalents 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. 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" and "Capital Resources and Funding Requirements."

Components of Our Results of Operations

Collaboration Revenue

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 primarily consists of collaboration revenue under our arrangements with our collaboration partners, including amounts that are recognized related to upfront payments, milestone payments and option exercise payments, amounts due to us for research and development services and reimbursement of certain expenses incurred. In the future, revenue may include additional milestone payments and option exercise payments, and royalties on any net product sales under our collaborations. In the near term, we expect that revenue may decrease as a result of the terminations of our collaboration agreements with Genentech and Novartis, effective in August 2025 and February 2026, respectively. In the future, 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, milestone and other payments, as well as the exercise or expiration of options.

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, 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 prepaid expenses and other current assets 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.

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, contract research organizations, or CROs, contractors and 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 discovery, platform and other 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 Cancer Research Technology Limited, or CRTL and Cancer Research UK, or the BT1718 Cancer Research UK Agreement, pursuant to which the Cancer Research UK Centre for Drug Development sponsored and funded a Phase I/IIa clinical trial for our previous product candidate, BT1718, in patients with advanced solid tumors. The costs incurred by Cancer Research UK were recorded as a liability in accordance with ASC 730, *Research and Development* as the payments were not based solely on the results of the research and development having future economic benefit. The accrual of the liability was recorded as incremental research and development expense in our consolidated statements of operations and comprehensive loss prior to the expiration and termination of the BT1718 Cancer Research UK Agreement in December 2024. See "Other Income (Expense)" for additional information on our accounting for the expiration and termination of the BT1718 Cancer Research UK Agreement.

Through our subsidiaries in the U.K., we receive reimbursements of certain research and development expenditures as part of a U.K. government research and development tax relief program. For 2023 and 2024, we benefitted from the Small and Medium-sized Enterprises, or SME, R&D Tax Relief program, under which we were able to surrender trading losses that arose from qualifying research and development expenses incurred by our subsidiaries in the U.K. for a cash rebate. The Finance Act 2024, which was enacted in February 2024, replaced the legacy research and development expenditure credit and the SME R&D Tax Relief program with a merged research and development expenditure credit scheme, or RDEC, and an enhanced research and development intensive support scheme, or ERIS. The Finance Act 2024 increased the cash rebate that may be claimed from 18.6% to 26.97% of qualifying expenditure and retroactively applied to qualifying expenditures incurred after April 1, 2023, if we qualify as "R&D intensive" for an accounting period (broadly, a loss-making SME whose relevant R&D expenditure represents, for accounting periods beginning on or after April 1, 2023, 40%, or, for accounting periods beginning on or after April 1, 2024, 30% of its total expenditure for that accounting period). For periods prior to April 1, 2023 the cash rebate was up to 33.35% of qualifying expenditures. We qualified as R&D intensive for the years ended December 31, 2025, 2024 and 2023. Going forward, if we no longer qualify as an R&D intensive SME during an accounting period, we will be subject to a single 20% gross rebate rate applying to all claims under the RDEC scheme.

For 2025 and beyond, the Finance Act 2024 also introduces restrictions (unless limited exceptions apply) on the tax relief that can be claimed for expenditures incurred on sub-contracted R&D activities or externally provided workers, where such sub-contracted activities are not carried out in the U.K. or such workers are not subject to U.K. payroll taxes. These restrictions may limit our ability to claim R&D tax credits for sub-contracted R&D in the future.

The U.K. research and development tax credit 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 it is not reflected as part of the income tax provision.

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 decrease in the near term as a result of our cost saving initiatives and our strategic reprioritization announced in March 2026. However, our research and development expenses will increase over the longer term if and as we: (i) continue the clinical development and seek to obtain marketing approval for our product candidates; (ii) initiate clinical trials for our product candidates; 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:

- identifying new product candidates to add to our development pipeline, including expanding our pipeline of Bicycle radioligand molecules and next-generation BDC molecules;
- completing research and preclinical development of our product candidates;
- establishing an appropriate safety profile with IND-enabling studies to advance our preclinical programs into clinical development;
- successful enrollment in, and the initiation and completion of clinical trials, including conducting future clinical trials of nuzefatide pevedotin and BT1702;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- commercializing our 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, the European Medicines Agency, or 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. In addition, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the current EU pharmaceutical legislation. The proposed revisions remain to be agreed and adopted by the European Council. Moreover, on December 1, 2024, a new European Commission took office. The proposal could, therefore, still be subject to revisions. If adopted in the form proposed, the European Commission proposals may result in a decrease in data and market exclusivity opportunities for our product candidates in the EU and make them open to generic or biosimilar competition earlier than is currently the case with a related reduction in reimbursement status.

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, commercial and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, insurance, 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 applicable functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the remeasurement at period-end exchange rates in foreign currencies are recorded in general and administrative expense in the consolidated statements 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 decrease in the near term as a result of our cost saving initiatives and our strategic reprioritization announced in March 2026. However, we expect that our general and administrative expenses may increase in the future if and 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 continue to incur increased expenses associated with being a public company including costs of accounting, audit, information systems, legal, intellectual property, regulatory and tax compliance services, director and officer insurance and investor and public relations.

Other Income (Expense)

Interest and Other Income

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

Interest Expense

Interest expense consists primarily of interest expense for financing arrangements.

Loss on Extinguishment of Debt

Loss on extinguishment of debt is related to the loss recognized from the repayment and voluntary termination of the Loan Agreement on July 9, 2024.

Gain on Extinguishment of Research and Development Funding Liability

Gain on extinguishment of research and development funding liability is related to the gain recognized from the extinguishment of the research and development funding liability previously recognized under the BT1718 Cancer Research UK Agreement. In December 2024, we entered into an Expiry and Revenue Sharing Agreement, or the BT1718 Expiration Agreement, with CRTL and Cancer Research UK pursuant to which, among other things, the BT1718 Cancer Research UK Agreement, and all rights and obligations (other than certain surviving provisions as outlined in the agreement) under the BT1718 Cancer Research UK Agreement, expired and terminated. As such, we recognized a gain on extinguishment of the research and development funding liability of $4.5 million during the year ended December 31, 2024, which is recorded within other income, net, in the consolidated statements of operations and comprehensive loss.

Provision For (Benefit From) Income Taxes

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

After consideration of our history of cumulative net losses in the U.K., we have concluded that it is more likely than not that we will not realize the benefits of our U.K. deferred tax assets and accordingly we have provided a valuation allowance for the full amount of the net deferred tax assets in the U.K. We intend to continue to maintain a full valuation allowance on our 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 incremental benefit from income taxes in 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 we are able to actually achieve.

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.

Results of Operations

The following table summarizes our results of operations for the years ended December 31, 2025, 2024 and 2023:

	Year Ended December 31,		
	2025	2024	2023
		(in thousands)	
Collaboration revenue	$ 72,586	$ 35,275	$ 26,976
Operating expenses:			
Research and development	240,283	172,966	156,496
General and administrative	79,368	72,181	60,426
Total operating expenses	319,651	245,147	216,922
Loss from operations	(247,065)	(209,872)	(189,946)
Other income (expense):			
Interest and other income	28,463	34,284	14,002
Interest expense	(206)	(1,730)	(3,263)
Loss on extinguishment of debt	—	(954)	—
Gain on extinguishment of research and development funding liability	—	4,476	—
Total other income, net	28,257	36,076	10,739
Net loss before income tax provision	(218,808)	(173,796)	(179,207)
Provision for (benefit from) income taxes	152	(4,765)	1,457
Net loss	$ (218,960)	$ (169,031)	$ (180,664)

Comparison of the Years Ended December 31, 2025 and 2024

	Year Ended December 31,		
	2025	2024	Change
		(in thousands)	
Collaboration revenue	$ 72,586	$ 35,275	$ 37,311
Operating expenses:			
Research and development	240,283	172,966	67,317
General and administrative	79,368	72,181	7,187
Total operating expenses	319,651	245,147	74,504
Loss from operations	(247,065)	(209,872)	(37,193)
Other income (expense):			
Interest and other income	28,463	34,284	(5,821)
Interest expense	(206)	(1,730)	1,524
Loss on extinguishment of debt	—	(954)	954
Gain on extinguishment of research and development funding liability	—	4,476	(4,476)
Total other income, net	28,257	36,076	(7,819)
Net loss before income tax provision	(218,808)	(173,796)	(45,012)
Provision for (benefit from) income taxes	152	(4,765)	4,917
Net loss	$ (218,960)	$ (169,031)	$ (49,929)

Collaboration Revenue

Collaboration revenue increased by $37.3 million in the year ended December 31, 2025, compared to the year ended December 31, 2024, primarily due to increases of $38.8 million from our collaboration with Novartis primarily due to the recognition of all remaining revenue upon a notice of termination from Novartis in November 2025, effective in February 2026, as well as $5.5 million from our collaboration with Bayer primarily due to the recognition of revenue

upon a notice of termination from Bayer of one of the target programs in November 2025, effective in January 2026. These increases were offset by a decrease in revenue of $6.9 million from our collaboration with Ionis due to the completion of the combined licenses and research and discovery performance obligation during the year ended December 31, 2024.

Research and Development Expenses

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

	Year Ended December 31,		
	2025	2024	Change
		(in thousands)	
Zelenectide pevedotin (Nectin-4)	$ 126,780	$ 82,705	$ 44,075
Nuzefatide pevedotin (EphA2)	8,487	9,119	(632)
Bicycle tumor-targeted immune cell agonists	1,991	7,840	(5,849)
Discovery, platform and other expense	43,221	30,293	12,928
Employee and contractor related expenses	69,701	58,687	11,014
Share-based compensation	18,024	19,424	(1,400)
Facility expenses	6,999	8,105	(1,106)
Research and development incentives and government grants	(34,920)	(43,207)	8,287
Total research and development expenses	$ 240,283	$ 172,966	$ 67,317

Research and development expenses increased by $67.3 million in the year ended December 31, 2025 compared to the year ended December 31, 2024, primarily due to increases of: $44.1 million in clinical program expenses for zelenectide pevedotin primarily due to the Phase II/III Duravelo-2 registrational trial as well as the Phase I/II clinical trials assessing zelenectide pevedotin in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer, which commenced recruiting patients in the first and third quarters of 2025, respectively; $12.9 million in discovery, platform and other expense primarily due to continued development of our pipeline programs, including advancing our Bicycle radioligand molecule pipeline; $11.0 million in employee and contractor related expenses primarily attributable to higher headcount prior to our August 2025 workforce reduction as well as $2.2 million in incremental severance-related costs period over period; and $8.3 million resulting from a decrease in research and development incentives primarily due to the retroactive impact of U.K. R&D tax credit reimbursement rate changes that were enacted and effective in the first quarter of 2024, retroactively applied to April 1, 2023. These increases were offset by decreases of: $5.8 million in Bicycle TICA program development expenses due to the timing of clinical program activities; $1.4 million in share-based compensation expense primarily due to the impact of our workforce reduction in August 2025; and $1.1 million in facility expenses.

We begin to separately track program expenses at candidate nomination, at which point we accumulate all direct external program costs incurred to support that program to date. Through December 31, 2025, we have incurred approximately $283.4 million and $57.2 million of direct external expenses for the development of zelenectide pevedotin and nuzefatide pevedotin, respectively, since their candidate nominations, and an aggregate of $51.3 million of direct external expenses for the development of the two named Bicycle TICA candidates since their nominations.

General and Administrative Expenses

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

	Year Ended December 31,		Change
	2025	2024	
	(in thousands)		
Personnel-related costs	$ 28,358	$ 23,500	$ 4,858
Professional and consulting fees	20,646	20,258	388
Other general and administration costs	9,577	9,047	530
Share-based compensation	21,440	18,657	2,783
Effect of foreign exchange rates	(653)	719	(1,372)
Total general and administrative expenses	$ 79,368	$ 72,181	$ 7,187

General and administrative expenses increased by $7.2 million in the year ended December 31, 2025 compared to the year ended December 31, 2024 primarily due to increases of $4.9 million in personnel-related costs primarily associated with higher headcount prior to our August 2025 workforce reduction as well as $1.6 million in incremental severance-related costs period over period, and $2.8 million in share-based compensation primarily associated with equity grants issued since the prior year, offset by a favorable impact of $1.4 million due to the effect of foreign exchange rates.

Other Income, net

Other income, net decreased by $7.8 million in the year ended December 31, 2025 compared to the year ended December 31, 2024, which was primarily due to a decrease in interest and other income of $5.8 million related to lower average interest rates period over period as well as higher cash and cash equivalents balances in the second half of 2024. In addition, during the year ended December 31, 2024, we recorded a gain on extinguishment of the research and development funding liability of $4.5 million recognized in the fourth quarter of 2024 as a result of the termination of our arrangement with Cancer Research UK for BT1718. These impacts were offset by a decrease in interest expense of $1.5 million due to the repayment and voluntary termination of the Loan Agreement in July 2024 and the loss on extinguishment of debt of $1.0 million recognized in the third quarter of 2024.

Provision For (Benefit From) Income Taxes

The provision for income taxes of $0.2 million for the year ended December 31, 2025, is primarily the result of the reversal of deferred tax assets for share-based payments resulting from our August 2025 workforce reduction. The benefit from income taxes of $4.8 million for the year ended December 31, 2024, 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, including income tax benefits of approximately $3.5 million recognized during the third quarter of 2024 related to the completion of a U.S. research and development tax credit study.

Liquidity and Capital Resources

Liquidity

From our inception in 2009 through December 31, 2025, 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 our equity securities, proceeds received from upfront payments, payments for research and development services and development milestone payments pursuant to our collaboration agreements, and borrowings pursuant to our Loan Agreement with Hercules.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2025, 2024 and 2023:

	Year Ended December 31,		
	2025	2024	2023
	(in thousands)		
Net cash used in operating activities	$ (249,675)	$ (164,724)	$ (60,628)
Net cash used in investing activities	(2,350)	(1,235)	(2,929)
Net cash (used in) provided by financing activities	(131)	519,750	250,027
Effect of exchange rate changes on cash	804	(694)	1,346
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (251,352)	$ 353,097	$ 187,816

Operating Activities

Net cash used in operating activities for the year ended December 31, 2025 was $249.7 million as compared to $164.7 million for the year ended December 31, 2024. The increase in cash used in operations of $85.0 million is primarily due to an increase in cash payments for clinical program activities, primarily related to the multiple clinical trials for zelenectide pevedotin, including for the Phase II/III registrational trial in patients with untreated and previously treated metastatic urothelial cancer and the initiation of the Phase I/II clinical trials in patients with NECTIN4 amplified advanced breast cancer and NECTIN4 amplified advanced or metastatic non-small cell lung cancer.

Investing Activities

During the years ended December 31, 2025 and 2024, we used $2.4 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, 2025, net cash used in financing activities was $0.1 million, primarily consisting of payments of finance lease obligations.

During the year ended December 31, 2024, net cash provided by financing activities was $519.8 million, primarily consisting of net proceeds of $544.1 million from the private placement completed in May 2024 and $7.5 million from the exercise of share options, offset by payments on debt of $31.9 million associated with the repayment and voluntary termination of the Loan Agreement.

At-the-Market Program

On June 5, 2020, we entered into a Controlled Equity Offering[SM] Sales Agreement, or the Sales Agreement, with Cantor Fitzgerald & Co. and Oppenheimer & Co. Inc., collectively, the Sales Agents, with respect to an at-the-market, or ATM, program pursuant to which we may offer and sell through the Sales Agents, from time to time at our sole discretion, ADSs. Our prospectus supplement dated May 26, 2023, related to our ADSs issuable pursuant to the Sales Agreement is not currently effective. Accordingly, we will not make any sales of our securities pursuant to the Sales Agreement unless and until a new prospectus, prospectus supplement or a new registration statement is filed. No ADSs were issued or sold pursuant to the Sales Agreement during the year ended December 31, 2025.

Loan Agreement

On July 9, 2024, we repaid all amounts outstanding, including $30.0 million in outstanding borrowings, $0.1 million in accrued and unpaid interest, an end-of-term charge of $1.5 million and a prepayment charge of $0.3 million, for a total aggregate payment of $31.9 million, and terminated the Loan Agreement. Upon the termination of the Loan Agreement, all security interests granted to the secured parties thereunder were terminated and released. For additional information on the Loan Agreement, see Note 6. "Debt" of our consolidated financial statements included elsewhere in this Annual Report.

Capital Resources and Funding Requirements

Our material cash requirements include expenses associated 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 continuing current trials and conducting future clinical trials of nuzefatide pevedotin and BT1702;
- seek to identify and develop additional product candidates, including expanding our pipeline of Bicycle radioligand molecules and next-generation BDC molecules;
- develop the necessary processes, controls and manufacturing data to seek 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.

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.

In addition, the following table summarizes our contractual obligations as of December 31, 2025 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods. For additional information, see Note 11. "Commitments and contingencies" of our consolidated financial statements.

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	3 years to 5 years	More than 5 years
			(in thousands)		
Operating lease commitments[1]	$ 19,814	$ 3,463	$ 6,528	$ 7,308	$ 2,515
Finance lease commitments	1,028	274	548	206	—
Total	$ 20,842	$ 3,737	$ 7,076	$ 7,514	$ 2,515

(1) Amounts reflect minimum payments due for our office and laboratory space leases. We have one office and laboratory lease in Cambridge, U.K. under an operating lease with a lease term through December 2031. We have two office and laboratory leases in Massachusetts, U.S. under operating leases that expire in March 2026 and December 2027.

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 above since the contracts are generally cancelable with advanced written notice, generally with a notice period of 90 days or less. From the time of notice until termination, we are contractually obligated to make certain minimum payments to the vendors, based on the timing of the notification and the exact terms of the agreement.

We have also entered into separate agreements with third parties which provide for various future milestone payments upon the achievement of specified development, regulatory, commercial and sales-based milestones with an aggregate total value of $105.8 million, as well as potential future royalty and other payments at percentages ranging from very low to low single digits. These additional milestone payments are contingent upon future events that are not considered probable of achievement as of December 31, 2025. As of December 31, 2025, we were unable to estimate the timing or likelihood of achieving these milestones.

As of December 31, 2025, we had cash and cash equivalents of $628.1 million. We expect that our existing cash and cash equivalents 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.

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:

- our ability to raise capital in light of the impacts of the unfavorable global economic and political conditions;
- 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 ongoing or future collaborations;

- 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, ownership interests of existing holders of our ADSs and ordinary shares will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our ADSs or ordinary shares. 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. Future debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt. Any debt or equity financing that we raise may contain terms that are not favorable to us or our shareholders.

Global trade disruption, volatility in the capital markets and continued uncertainty may contribute to a general global economic slowdown or recession. Inflationary factors, such as increases in the cost of our clinical trial materials and supplies, interest rates and overhead costs may adversely affect our operating results. In addition, current or future tariffs or other trade barriers may result in increased research and development expenses, including with respect to increased costs associated with active pharmaceutical ingredients, raw materials, laboratory equipment and research materials and components. High interest rates also present a recent challenge impacting the U.S. economy and could make it more difficult for us to obtain traditional financing on acceptable terms, if at all, in the future. Furthermore, such economic conditions have produced downward pressure on share prices. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, in the future increased inflation rates and macroeconomic turmoil may adversely affect us by increasing our costs and the costs of our CMOs and other suppliers. In addition, our labor and research and development costs may increase due to supply chain constraints, consequences associated with geopolitical conflicts, war, worsening global macroeconomic conditions, including those resulting from changes in global trade policies, or other factors, which may result in additional stress on our working capital resources. 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.

Critical Accounting 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 this Annual Report, 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 Revenue

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 and/or optimizing compounds for further development and commercialization, (ii) the transfer of intellectual property rights (licenses), or (iii) options to obtain additional research and development services or licenses for additional targets, or to optimize product candidates, upon the payment of option fees.

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 and reimbursement of certain expenses incurred; 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 Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers,* or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, 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 we transfer to the customer.

As part of the accounting for these arrangements, we must make significant judgments, including identifying performance obligations in the contract, including assessing whether options to additional goods or services provide a material right to the customer, estimating the amount of variable consideration to include in the transaction price, allocating the transaction price to each performance obligation based on estimated relative standalone selling prices, and measuring progress towards the satisfaction of each performance obligation.

Many of our performance obligations, whether distinct or combined, do not have readily available standalone selling prices and therefore we are required to make judgments and estimates regarding the standalone selling prices utilizing key assumptions, which may include other comparable transactions, pricing considered in negotiating the transaction, probabilities of technical and regulatory success and estimated costs. We evaluate the measure of progress each reporting period and, if necessary, adjust 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 an arrangement. In addition, we must determine whether a change in scope or price of a contract represents a contract modification and, if so, account for the effects of the modification when it is approved by both parties to the contract. We determine the accounting for a contract modification as (i) a separate contract if the

modification adds distinct goods or services and the price of the contract increases by an amount that reflects the standalone selling price of those additional goods or services; (ii) a termination of the existing contract and creation of a new contract if the remaining goods or services are distinct from those transferred before the modification; (iii) a cumulative catch-up adjustment to the revenue recognized on the original contract if the remaining goods or services are not distinct from those transferred before the modification; or (iv) a combination of (ii) and (iii) if the remaining goods or services include both goods and services that are distinct from those transferred before the modification and goods and services that are not distinct.

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 the portion of the transaction price that is allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license to our intellectual property is distinct from the other promises in the arrangement, 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 license for its intended purpose without the receipt of the remaining promises, whether the value of the license 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. 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.

Customer Options: A customer's right to choose, at its discretion, to make a payment for additional goods or services is generally considered an option. If we are not presently obligated to provide, and do not have a right to consideration for delivering additional goods or services, the item is considered an option. 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 goods and 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 goods and 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. Milestone payments that may only be achieved after the exercise of a customer option are excluded from the initial determination of the transaction price.

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.

Accrued External Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued external 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 external research and development expenses include costs associated with:

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

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. Our historical accrual estimates have not been materially different from actual costs, and as of December 31, 2025, there have not been any material adjustments to our prior estimates of accrued external research and development expenses.

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

Interest Rate Sensitivity

As of December 31, 2025, we had cash and cash equivalents of $628.1 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest and treasury rates. Our surplus cash has been invested in money market funds that invest primarily in short-term, highly liquid securities and that maintain a stable net asset value. 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. Our earnings would be affected by changes in interest rates due to the impact those changes have on interest income generated from our cash and cash equivalents. We believe we have minimal interest rate risk as a one percentage point change in the average interest rate on our portfolio would not have a material effect on our consolidated statements of operations and comprehensive loss for the year ended December 31, 2025.

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, or USD. 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 consolidated financial statements are presented in USD. The functional currency of our 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 $0.7 million for the year ended December 31, 2025 and foreign exchange losses of $0.7 million and $0.6 million for the years ended December 31, 2024 and 2023, 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 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 currency translation adjustment included in the consolidated statements of shareholders' equity and as a component of accumulated other comprehensive income (loss) in the consolidated balance sheets.

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.

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, 2025. Based on the evaluation of our disclosure controls and procedures as of December 31, 2025, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective.

Management's Report on Internal Control over Financial Reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate. Our internal control over financial reporting is a process designed under the supervision of our principal executive officer and principal financial officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

Our management conducted an assessment of our internal control over financial reporting based on the framework established in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013). Based on the assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2025.

Attestation Report of the Registered Public Accounting Firm

We are a non-accelerated filer and a smaller reporting company, and therefore our independent registered public accounting firm has not issued an attestation report on the effectiveness of internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

Insider Trading Arrangements

During the three months ended December 31, 2025, our directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) adopted or terminated the contracts, instructions or written plans for the purchase or sale of our securities set forth in the table below, each of which is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act ("Rule 10b5-1 Plan").

			Type of Trading Arrangement			
Name and Position	Action	Adoption/Termination Date	Rule 10b5-1	Non-Rule 10b5-1	Total Number of Ordinary Shares to be Sold	Expiration Date
Charles Swanton, Director[(1)]	Termination	December 22, 2025	X		3,500	July 14, 2028

(1) On December 22, 2025, Charles Swanton, a member of our board of directors, terminated a pre-arranged share trading plan pursuant to Rule 10b5-1, which was adopted on October 14, 2024. The plan provided for the sale of Restricted Share Units that were expected to vest during the term of the 10b5-1 plan until July 14, 2028 or the earlier completion of all authorized transactions under the plan.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not Applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

Information About Our Directors and Executive Officers

The information required by this item will be contained in our Proxy Statement under the captions "Board of Directors and Corporate Governance—Board of Directors" and "Executive Officers of the Company" and is incorporated herein by reference.

Identification of Audit Committee and Financial Experts

Information regarding our Audit Committee required by this item will be contained in our Proxy Statement under the caption "Board of Directors and Corporate Governance—Corporate Governance—Committees of our Board of Directors—Audit Committee," and is hereby incorporated by reference.

Material Changes to Procedures for Recommending Directors

Information regarding procedures for recommending directors required by this item will be contained in our Proxy Statement under the caption "Board of Directors and Corporate Governance—Corporate Governance—Committees of our Board of Directors—Nominating and Corporate Governance Committee—Shareholder Recommendations and Nominees," and is hereby incorporated by reference.

Code of Business Conduct and Ethics

Information regarding our Code of Business Conduct and Ethics required by this item will be contained in our Proxy Statement under the caption "Board of Directors and Corporate Governance—Corporate Governance—Code of Business Conduct and Ethics," and is hereby incorporated by reference. The full text of our Code of Business Conduct and Ethics is available at the investors section of our website at www.bicycletherapeutics.com. If we make any amendments to our Code of Business Conduct and Ethics, or grant any waiver from a provision of our Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this Annual Report.

Delinquent Section 16(a) Reports

Information regarding compliance with Section 16(a) of the Exchange Act required by this item will be contained in our Proxy Statement under the caption "Delinquent Section 16(a) Reports," if any, and is hereby incorporated by reference.

Insider Trading Policy

We adopted insider trading policies and procedures governing the purchase, sale, and/or other dispositions of our ordinary shares by directors, officers, employees and consultants that are reasonably designed to promote compliance with insider trading laws, rules and regulations, and any applicable listing standards. It is our policy to comply with all applicable laws and regulations relating to insider trading in connection with the repurchase of our securities. A copy of our Amended and Restated Insider Trading Policy, as amended, is filed as Exhibit 19.1 to this report.

ITEM 11. EXECUTIVE COMPENSATION.

Information regarding our executive compensation required by this item will be contained in our Proxy Statement under the captions "Executive Compensation," "Pay Versus Performance" and "Director Remuneration," and is hereby incorporated by reference.

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

The information required by this item will be contained in our Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" and is hereby incorporated by reference.

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

The information required by this item will be contained in our Proxy Statement under the captions "Board of Directors and Corporate Governance—Corporate Governance—Board Independence" and "Transactions with Related Persons" and is hereby incorporated by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

Information regarding accounting fees and services required by this item will be contained in our Proxy Statement in the Proposal titled "Ratification of the Appointment of PricewaterhouseCoopers LLP as our Independent Registered Public Accounting Firm for the Year Ending December 31, 2026" under the captions "Independent Registered Public Accounting Firm Fees" and "Pre-Approval Policies and Procedures" and is hereby incorporated by reference.

PART IV

ITEM 15. EXHIBITS AND 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

(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 Annual Report other than Exhibit 32.1, which shall be deemed furnished:

Number	Description
3.1	Articles of Association, dated May 16, 2024 (incorporated by reference to Exhibit 3.1 to the Quarterly Report on Form 10-Q (File No. 001-38916) filed with the Securities and Exchange Commission on August 6, 2024).
4.1	Form of Deposit Agreement (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the 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 Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
4.3	Letter Agreement, dated July 1, 2020, between Bicycle Therapeutics plc and Citibank, N.A. (incorporated by reference to Exhibit 4.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on November 5, 2020).
4.4	Amendment to Letter Agreement, dated October 27, 2020, between Bicycle Therapeutics plc and Citibank, N.A. (incorporated by reference to Exhibit 4.4 to Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on March 11, 2021).

Number	Description
4.5	Amendment to Letter Agreement, dated May 24, 2021, between Bicycle Therapeutics plc and Citibank, N.A. (incorporated by reference to Exhibit 4.1 to Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on August 5, 2021).
4.6	Description of Securities (incorporated by reference to Exhibit 4.6 to the Registrant's Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.1+	Form of Share Option Contract of Bicycle Therapeutics Limited for employees in England (incorporated by reference to Exhibit 10.2 to the 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 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 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 (incorporated by reference to Exhibit 10.4 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on March 10, 2020).
10.5+	2019 Employee Share Purchase Plan (incorporated by reference to Exhibit 10.5 to Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
10.6+	Amended and Restated Bicycle Therapeutics plc 2020 Equity Incentive Plan, or the 2020 Plan and forms of awards thereunder (incorporated by reference to Exhibit 10.6 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 28, 2023).
10.7+	Amendment No. 1 to the Amended and Restated 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Quarterly Report on Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on August 8, 2025).
10.8+	Form of Option Grant Notice and Agreement (for employees) for the 2020 Plan (incorporated by reference to Exhibit 10.7 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.9+	Form of Option Grant Notice and Agreement (for non-employees) for the 2020 Plan (incorporated by reference to Exhibit 10.8 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.10+	Form of Restricted Share Unit Grant Notice and Agreement (for employees) for the 2020 Plan (incorporated by reference to Exhibit 10.9 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.11+	Form of Amended and Restated Restricted Share Unit Grant Notice and Agreement (for employees) for the 2020 Plan (incorporated by reference to Exhibit 10.10 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).

Number	Description
10.12+	Form of Restricted Share Unit Grant Notice and Agreement (regular settlement for directors) for the 2020 Plan (incorporated by reference to Exhibit 10.11 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.13+	Form of Amended and Restated Restricted Share Unit Grant Notice and Agreement (regular settlement for directors) for the 2020 Plan (incorporated by reference to Exhibit 10.12 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.14+	Form of Restricted Share Unit Grant Notice and Agreement (deferred settlement for directors) for the 2020 Plan (incorporated by reference to Exhibit 10.13 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.15+	Form of Amended and Restated Restricted Share Unit Grant Notice and Agreement (deferred settlement for directors) for the 2020 Plan (incorporated by reference to Exhibit 10.14 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 25, 2025).
10.16+	Bicycle Therapeutics plc 2024 Inducement Plan, or the 2024 Plan (incorporated by reference to Exhibit 99.1 to the Registration Statement on Form S-8 (File No. 333-281304), filed with the Securities and Exchange Commission on August 6, 2024).
10.17+	Form of Option Grant Notice and Option Agreement for the 2024 Plan (incorporated by reference to Exhibit 99.2 to the Registration Statement on Form S-8 (File No. 333-281304), filed with the Securities and Exchange Commission on August 6, 2024).
10.18+	Form of RSU Grant Notice and RSU Agreement for the 2024 Plan (incorporated by reference to Exhibit 99.3 to the Registration Statement on Form S-8 (File No. 333-281304), filed with the Securities and Exchange Commission on August 6, 2024).
10.19+	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.4 to Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
10.20+	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).
10.21+	Amendment No. 1 to Service Agreement, dated July 24, 2023, by and between BicycleTx Limited and Kevin Lee (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q (File No. 001-38916) filed with the Securities and Exchange Commission on November 2, 2023).
10.22+	Amended and Restated Employment Agreement, dated September 26, 2019, by and between BicycleTx Ltd. and Michael Skynner, Ph.D. (incorporated by reference to Exhibit 10.9 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on March 10, 2020).
10.23+	Amended and Restated Employment Agreement, dated January 6, 2022, by and between BicycleTx Ltd. And Michael Skynner, Ph.D. (incorporated by reference to Exhibit 10.11 to the Annual Report on Form 10-K(File No. 001-38916), filed with the Securities and Exchange Commission on March 1, 2022).
10.24+	Amendment No. 2 to Service Agreement, dated February 20, 2023, by and between BicycleTx Limited and Michael Skynner (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on May 4, 2023).

Number	Description
10.25+	Service Agreement, dated March 18, 2024, by and between BicycleTx Ltd. and Michael Charles Ferguson Hannay (incorporated by reference to Exhibit 10.4 to the Quarterly Report on Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on August 6, 2024).
10.26+	Form of letter agreement to amend Service Agreement by and between the BicycleTx Ltd. and its executive officers in the United Kingdom, effective January 1, 2020 (incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on May 7, 2020).
10.27+	Form of letter agreement to amend Service Agreement by and between the BicycleTx Ltd. and its executive officers in the United Kingdom, effective January 1, 2021 (incorporated by reference to Exhibit 10.27 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on March 11, 2021).
10.28+	Service Agreement, dated January 5, 2022, by and between BicycleTx Ltd. and Alistair Milnes (incorporated by reference to Exhibit 10.17 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on March 1, 2022).
10.29+	Amendment No. 1 to Service Agreement, dated February 20, 2023, by and between BicycleTx Limited and Alistair Milnes (incorporated by reference to Exhibit 10.6 to the Quarterly Report on Form 10-Q (File No. 001-38916), filed with the Securities and Exchange Commission on May 4, 2023).
10.30+	Form of Deed of Indemnity between the Company and each of its directors (incorporated by reference to Exhibit 10.1 to Current Report on Form 8-K (File No. 001-38916), filed with the Securities and Exchange Commission on November 12, 2019).
10.31+	Form of Deed of Indemnity between the registrant and each of its executive officers (incorporated by reference to Exhibit 10.2 to Current Report on Form 8-K (File No. 001-38916), filed with the Securities and Exchange Commission on November 12, 2019).
10.32+	Non-Employee Director Compensation Policy, as amended as of December 11, 2025.
10.33	Registration Rights Agreement, dated as of April 18, 2024, by and among Bicycle Therapeutics plc and 667 L.P. and Baker Brothers Life Sciences L.P. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K (File No. 001-38916) filed with the Securities and Exchange Commission on April 18, 2024).
10.34	Securities Purchase Agreement, dated as of May 23, 2024, by and among Bicycle Therapeutics plc and purchasers named therein (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 May 23, 2024).
19.1	Amended and Restated Insider Trading Policy, as amended October 1, 2025.
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.

Number	Description
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.
97.1	Incentive Compensation Recoupment Policy (incorporated by reference to Exhibit 97.1 to the Annual Report on Form 10-K (File No. 001-38916), filed with the Securities and Exchange Commission on February 20, 2024).
101.INS	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema with Embedded Linkbase Documents.
104	Cover page interactive data file (formatted as Inline XBRL and contained in Exhibit 101)

* 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.

ITEM 16. FORM 10-K SUMMARY

None.

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, 2025 and 2024, and the related consolidated statements of operations and comprehensive loss, of shareholders' equity and of cash flows for each of the three years in the period ended December 31, 2025, 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, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025 in conformity with accounting principles generally accepted in the United States of America.

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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that (i) relate to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

External research and development expenses

As described in Note 2 and 5 to the consolidated financial statements, research and development expenses were $240.3 million for the year ended December 31, 2025, of which a significant portion related to external research and development expense. Accrued external research and development expenses were $20.5 million as of December 31, 2025. The Company has entered into various research and development and manufacturing contracts, including contracts with respect to preclinical studies and clinical trials. Research and development costs are expensed as incurred. Significant judgments and estimates are made by management in estimating external research and development expenses incurred and associated accrued balance at the end of the reporting period.

For estimating accrued external research and development expenses, management analyzes the progress of the research and development and manufacturing activities, including the level of service performed and associated cost incurred, invoices received and contracted costs.

The principal considerations for our determination that performing procedures relating to external research and development expenses is a critical audit matter are (i) the significant judgment by management in developing the estimate of the accrued external research and development expenses; and (ii) a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating management's significant assumption related to the level of service performed.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) reading significant research and development and manufacturing contracts; (ii) testing the external research and development expenses incurred, on a sample basis, by tracing information to the underlying contracts, purchase orders, invoices and information received from the research institutions or vendors, as applicable; (iii) testing management's process for estimating the accrued external research and development expenses; (iv) testing the completeness and accuracy of underlying data used by management; and (v) evaluating the reasonableness of the significant assumption used by management in estimating of the level of service performed on a sample of contracts. Evaluating management's assumption related to the level of service performed involved obtaining and examining a sample of third party contracts to evaluate the completeness and consistency of the costs and milestones in the contract with those used in developing the estimate, testing the associated cost incurred based on underlying contracts and other information received from research organizations and re-calculating the level of service performed for a study or research and development activity.

Accounting for termination of Novartis Collaboration Agreement

As described in Note 9 to the consolidated financial statements, in November 2025, Novartis Pharma AG ("Novartis") provided the Company with a notice of termination of the Novartis Collaboration Agreement in its entirety, effective in February 2026. Management exercised significant judgment in concluding that the notice of termination should be accounted for as a contract modification in the fourth quarter of 2025 as it reduces the scope of the arrangement. Management concluded that the notice of termination substantively removes all remaining performance obligations, including remaining material rights, as of the date of the notice as Novartis will not benefit from any remaining activities performed during the notice period and the likelihood of exercising any remaining options is remote. As a result, the Company recognized the remaining unrecognized transaction price of $41.9 million as revenue on the date of the notice of termination.

The principal considerations for our determination that performing procedures relating to accounting for the termination of Novartis Collaboration Agreement is a critical audit matter are (i) the significant judgment by management in determining the timing of accounting for the termination of collaboration agreement, and (ii) a high degree of auditor judgment, subjectivity and effort in performing procedures related to accounting for the termination of Novartis Collaboration Agreement.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) reading the Novartis Collaboration Agreement and the notice of termination; (ii) evaluating management's assessment of the accounting for the termination of the Novartis Collaboration Agreement; (iii) evaluating the reasonableness of significant judgment used by management related to the determination that Novartis will not benefit from any remaining activities performed during the notice period and the likelihood of exercising any remaining options is remote by evaluating its consistency with the contractual terms and considering the progress of the research as of the date of termination; and (iv) evaluating the sufficiency of the disclosures in the consolidated financial statements.

/s/ PricewaterhouseCoopers LLP
Cambridge, United Kingdom
March 17, 2026

We have served as the Company's auditor since 2010.

Bicycle Therapeutics plc
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 628,110	$ 879,520
Prepaid expenses and other current assets	19,181	13,432
Research and development incentives receivable	35,594	35,653
Total current assets	682,885	928,605
Property and equipment, net	6,021	9,516
Operating lease right-of-use assets	15,886	7,673
Other assets	12,805	11,074
Total assets	$ 717,597	$ 956,868
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 9,669	$ 15,793
Accrued expenses and other current liabilities	44,354	41,246
Deferred revenue, current portion	2,961	10,191
Total current liabilities	56,984	67,230
Operating lease liabilities, net of current portion	14,096	3,990
Deferred revenue, net of current portion	35,508	91,467
Other long-term liabilities	1,032	1,121
Total liabilities	107,620	163,808
Commitments and contingencies (Note 11)		
Shareholders' equity:		
Ordinary shares, including non-voting ordinary shares, £0.01 nominal value; 159,685,229 and 155,876,645 shares authorized at December 31, 2025 and December 31, 2024, respectively; 69,367,896 and 69,061,418 shares issued and outstanding at December 31, 2025 and December 31, 2024, respectively	894	890
Additional paid-in capital	1,512,339	1,472,842
Accumulated other comprehensive (loss) income	(3,505)	119
Accumulated deficit	(899,751)	(680,791)
Total shareholders' equity	609,977	793,060
Total liabilities and shareholders' equity	$ 717,597	$ 956,868

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,		
	2025	2024	2023
Collaboration revenue	$ 72,586	$ 35,275	$ 26,976
Operating expenses:			
Research and development	240,283	172,966	156,496
General and administrative	79,368	72,181	60,426
Total operating expenses	319,651	245,147	216,922
Loss from operations	(247,065)	(209,872)	(189,946)
Other income (expense):			
Interest and other income	28,463	34,284	14,002
Interest expense	(206)	(1,730)	(3,263)
Loss on extinguishment of debt	—	(954)	—
Gain on extinguishment of research and development funding liability	—	4,476	—
Total other income, net	28,257	36,076	10,739
Net loss before income tax provision	(218,808)	(173,796)	(179,207)
Provision for (benefit from) income taxes	152	(4,765)	1,457
Net loss	$ (218,960)	$ (169,031)	$ (180,664)
Net loss per share, basic and diluted	$ (3.16)	$ (2.90)	$ (5.08)
Weighted average ordinary shares outstanding, basic and diluted	69,279,838	58,207,593	35,592,362
Comprehensive loss:			
Net loss	$ (218,960)	$ (169,031)	$ (180,664)
Other comprehensive income (loss):			
Foreign currency translation adjustment	(3,624)	1,423	(1,691)
Total comprehensive loss	$ (222,584)	$ (167,608)	$ (182,355)

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

Bicycle Therapeutics plc
Consolidated Statements of Shareholders' Equity
(In thousands, except share amounts)

	Ordinary Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount				
Balance at December 31, 2022	29,873,893	$ 387	$ 601,105	$ 387	$ (331,096)	$ 270,783
Issuance of ADSs upon exercise of share options	54,023	—	681	—	—	681
Issuance of ADSs and non-voting ordinary shares, net of commissions and offering expenses of $16.0 million	12,384,706	162	249,183	—	—	249,345
Issuance of ADSs upon settlement of restricted share units	119,144	1	—	—	—	1
Share-based compensation expense	—	—	32,477	—	—	32,477
Foreign currency translation adjustment	—	—	—	(1,691)	—	(1,691)
Net loss	—	—	—	—	(180,664)	(180,664)
Balance at December 31, 2023	42,431,766	550	883,446	(1,304)	(511,760)	370,932
Issuance of ADSs upon exercise of share options	554,596	8	7,519	—	—	7,527
Issuance of ADSs and non-voting ordinary shares, net of commissions and offering expenses of $11.4 million	25,933,706	331	543,796	—	—	544,127
Issuance of ADSs upon settlement of restricted share units	141,350	1	—	—	—	1
Share-based compensation expense	—	—	38,081	—	—	38,081
Foreign currency translation adjustment	—	—	—	1,423	—	1,423
Net loss	—	—	—	—	(169,031)	(169,031)
Balance at December 31, 2024	69,061,418	890	1,472,842	119	(680,791)	793,060
Issuance of ADSs upon exercise of share options	10,116	—	33	—	—	33
Issuance of ADSs upon settlement of restricted share units	296,362	4	—	—	—	4
Share-based compensation expense	—	—	39,464	—	—	39,464
Foreign currency translation adjustment	—	—	—	(3,624)	—	(3,624)
Net loss	—	—	—	—	(218,960)	(218,960)
Balance at December 31, 2025	69,367,896	$ 894	$ 1,512,339	$ (3,505)	$ (899,751)	$ 609,977

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,		
	2025	**2024**	**2023**
Cash flows from operating activities:			
Net loss	$ (218,960)	$ (169,031)	$ (180,664)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	39,464	38,081	32,477
Depreciation and amortization	6,422	7,174	6,546
Non-cash interest	—	211	383
Loss on extinguishment of debt	—	954	—
Gain on extinguishment of research and development funding liability	—	(4,476)	—
Deferred income tax (benefit) provision	(850)	(5,226)	3,306
Other non-cash charges	—	1,036	661
Changes in operating assets and liabilities:			
Accounts receivable	—	—	2,482
Research and development incentives receivable	2,892	(11,947)	(3,684)
Prepaid expenses and other assets	(5,816)	(2,044)	(2,072)
Operating lease right-of-use assets	4,597	4,402	4,186
Accounts payable	(6,871)	3,095	8,002
Accrued expenses and other current liabilities	4,093	9,698	2,398
Operating lease liabilities	(5,456)	(4,888)	(4,109)
Deferred revenue	(69,190)	(31,952)	68,951
Other long-term liabilities	—	189	509
Net cash used in operating activities	(249,675)	(164,724)	(60,628)
Cash used in investing activities:			
Purchases of property and equipment	(2,350)	(1,235)	(2,929)
Net cash used in investing activities	(2,350)	(1,235)	(2,929)
Cash flows from financing activities:			
Repayment of debt	—	(31,863)	—
Proceeds from the issuance of ADSs and non-voting ordinary shares, net of issuance costs	—	544,127	249,345
Proceeds from the exercise of share options and settlement of restricted share units	37	7,528	682
Principal payments on finance lease obligations	(168)	(42)	—
Net cash (used in) provided by financing activities	(131)	519,750	250,027
Effect of exchange rate changes on cash, cash equivalents and restricted cash	804	(694)	1,346
Net (decrease) increase in cash, cash equivalents and restricted cash	(251,352)	353,097	187,816
Cash, cash equivalents and restricted cash at beginning of period	880,067	526,970	339,154
Cash, cash equivalents and restricted cash at end of period	$ 628,715	$ 880,067	$ 526,970
Reconciliation of cash, cash equivalents and restricted cash			
Cash and cash equivalents	$ 628,110	$ 879,520	$ 526,423
Restricted cash included in prepaid expenses and other current assets	547	—	—
Restricted cash included in other assets	58	547	547
Total cash, cash equivalents and restricted cash	$ 628,715	$ 880,067	$ 526,970
Supplemental disclosure of cash flow information			
Cash paid for interest on debt	$ —	$ 1,373	$ 2,753
Cash paid for interest on finance lease obligations	$ 78	$ 23	$ —
Cash (received from) paid for income taxes	$ (717)	$ 792	$ 562
Cash paid for amounts included in the measurement of operating lease liabilities	$ 5,957	$ 5,785	$ 5,595
Changes in purchases of property and equipment in accounts payable and accrued expenses	$ —	$ (4)	$ (1,744)
Non-cash impact to operating lease right-of-use assets and operating lease liabilities	$ 12,383	$ —	$ 3,898
Property and equipment obtained under finance leases	$ —	$ 1,102	$ —

The accompanying notes are an integral part of the 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 pharmaceutical company developing a novel class of medicines, which the Company refers to as Bicycle® molecules, for diseases that are underserved by existing therapeutics. Bicycle molecules 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 internal programs are focused on oncology indications with high unmet medical need.

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").

Liquidity

As of December 31, 2025, the Company had cash and cash equivalents of $628.1 million.

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 the sale of its equity securities, as well as proceeds received from its collaboration arrangements (Note 9) and proceeds from a loan agreement with Hercules Capital, Inc. ("Hercules") (Note 6). The Company has incurred recurring losses since inception, including net losses of $219.0 million, $169.0 million, and $180.7 million for the years ended December 31, 2025, 2024, and 2023, respectively. As of December 31, 2025, the Company had an accumulated deficit of $899.8 million. The Company expects to continue to generate operating losses in the foreseeable future. The Company expects that its cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the issuance date of these annual consolidated financial statements.

On May 23, 2024, the Company entered into a securities purchase agreement (the "Purchase Agreement") with purchasers named therein (the "Investors"). Pursuant to the Purchase Agreement, the Company sold 6,764,705 ADSs, representing the same number of ordinary shares, nominal value £0.01 per share, and 19,169,001 non-voting ordinary shares, nominal value £0.01 per share, each at a purchase price equal to $21.42 per share (the "Private Placement"). The Company completed the Private Placement on May 28, 2024. The transaction resulted in gross proceeds to the Company of $555.5 million, and after deducting commissions and offering expenses of $11.4 million, net proceeds to the Company of $544.1 million.

On July 17, 2023, the Company completed an underwritten public offering of its securities, pursuant to which the Company issued and sold 6,117,648 ADSs, representing the same number of ordinary shares, nominal value £0.01 per share, which included 1,411,764 ADSs sold upon the underwriters' full exercise of their option to purchase additional ADSs, and 4,705,882 non-voting ordinary shares, nominal value £0.01 per share, at a public offering price of $21.25 per ADS or non-voting ordinary share, respectively. The transaction resulted in gross proceeds to the Company of $230.0 million, and after deducting underwriting discounts, commissions, and offering expenses of $14.9 million, net proceeds to the Company of $215.1 million.

On June 5, 2020, the Company entered into a Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. and Oppenheimer & Co. Inc. (the "Sales Agents") with respect to an at-the-market ("ATM") program pursuant to which the Company may offer and sell through the Sales Agents, from time to time at the Company's sole discretion,

ADSs, each ADS representing one ordinary share. No ADSs were issued or sold pursuant to the Sales Agreement during the years ended December 31, 2025 and 2024. During the year ended December 31, 2023, the Company issued and sold 1,561,176 ADSs, representing the same number of ordinary shares for gross proceeds of $35.3 million, resulting in net proceeds of $34.2 million after deducting sales commissions and offering expenses of $1.1 million.

The Company expects its expenses to increase substantially in connection with ongoing activities, particularly if, and as, the Company advances its clinical trials for its product candidates in development and preclinical activities. Accordingly, the Company will need to obtain additional funding in connection with continuing operations. If the Company is unable to raise funding 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. 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.

The Company is subject to risks common to companies in the biotechnology and pharmaceutical industries, including but not limited to, risks of delays in initiating or continuing research programs and clinical trials, 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, if approved, 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.

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, revenue recognition, the accrual for research and development expenses and research and development incentives receivable, share-based compensation expense, valuation of right-of-use assets and liabilities, gain on extinguishment of research and development funding liability and income taxes, including the valuation allowance for deferred tax assets. 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.

Significant risks and uncertainties

The Company currently operates in a period of economic uncertainty which has been significantly impacted by domestic and global monetary and fiscal policy, changes to global trade policies, geopolitical conflicts and war, inflation and interest rates, and fluctuations in monetary exchange rates. While the Company has experienced limited financial impacts at this time, the Company continues to monitor these factors and events and the potential effects each may have on the Company's business, financial condition, results of operations and growth prospects.

Foreign currency and currency translation

The reporting currency of the Company is the U.S. Dollar ("USD"). The functional currency of Bicycle Therapeutics plc is the USD. 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 foreign currencies 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 $0.7 million for the year ended December 31, 2025, and foreign exchange losses of $0.7 million and $0.6 million for the years ended December 31, 2024 and 2023, respectively.

The Company translates the assets and liabilities of its non-U.S. subsidiaries 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 foreign currency translation adjustment, which is included in the consolidated statements of shareholders' equity as a component of accumulated other comprehensive (loss) income.

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 cash equivalents. 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 diversifies its cash and cash equivalents in multiple financial institutions and in money market funds and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships and investments in money market funds.

As of December 31, 2025 and 2024, the Company had no accounts receivable. For the years ended December 31, 2025, 2024, and 2023, the Company's revenue has been generated from collaboration agreements with Bayer Consumer Care AG ("Bayer"), Novartis Pharma AG ("Novartis"), Ionis Pharmaceuticals, Inc. ("Ionis"), Genentech, Inc. ("Genentech") and AstraZeneca AB ("AstraZeneca") (Note 9).

The Company relies, and expects to continue to rely, on multiple vendors to manufacture clinical trial materials 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, cash equivalents and restricted cash

The Company considers all highly liquid investments that are readily convertible to known amounts of cash with original maturities of three months or less at date of purchase to be cash equivalents. The Company had cash equivalents of $364.2 million and $664.9 million at December 31, 2025 and 2024, respectively.

As of December 31, 2025 and 2024, the Company had $0.5 million of restricted cash related to a collateralized letter of credit in connection with the Company's lease for office and laboratory space in Cambridge, Massachusetts, which is included within prepaid expenses and other current assets, and other assets, respectively, in the Company's consolidated balance sheet.

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 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 and software	3 years
Furniture and office equipment	3 to 5 years

Costs for property and equipment 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. To date, there have been no significant asset retirements. Expenditures for repairs and maintenance are charged to expense as incurred.

Impairment of long-lived assets

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 may 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 material impairment losses on long-lived assets.

Fair value measurements

Certain of the Company's assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted prices in active markets for identical assets or liabilities.
- Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 — Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The carrying values of cash, cash equivalents and restricted cash, research and development incentives receivable, prepaid expenses and 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.

Debt issuance costs

Debt issuance costs consist of certain third-party legal expenses and payments made to secure commitments under certain debt financing arrangements. These amounts are recorded as a reduction to the carrying value of the associated debt and are recognized as interest expense over the period of the financing arrangement.

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 operates and manages its business as a single operating segment, which is developing a unique class of chemically synthesized medicines based on its proprietary platform.

The Company operates in two geographic regions: the United Kingdom and the United States.

For additional segment information, see Note 15, "Segments and geographic information."

Leases

Leases are accounted for in accordance with Accounting Standards Codification ("ASC") Topic 842, *Leases* ("ASC 842"). The Company determines if an arrangement is or contains a lease at inception. Assets and liabilities related to operating leases are included in operating lease right of use ("ROU") assets, accrued expenses and other current liabilities, and operating lease liabilities, net of current portion, in the Company's consolidated balance sheets. Assets and liabilities related to finance leases are included in property and equipment, net, accrued expenses and other current liabilities, and other long-term liabilities in the consolidated balance sheet.

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 on the lease commencement date based on the present value of lease payments over the lease term. The ROU asset also includes lease payments made before the lease commencement date and excludes any lease incentives. The Company identifies and assesses the following significant assumptions in recognizing the ROU assets and corresponding lease liabilities:

- *Expected lease term* – The expected lease term includes both contractual lease periods and, when applicable, periods covered by an option to extend the lease when it is reasonably certain that the Company will exercise the extension option, or cancelable option periods when it is reasonably certain that the Company would not exercise such cancelation option.

- *Incremental borrowing rate* – As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available on the commencement date in determining the present value of lease payments. As the Company does not have any external borrowings for comparable terms of its leases, the Company estimates the incremental borrowing rate by comparing interest rates available in the market for similar borrowings and third-party quotations.

- *Lease and non-lease components* – The Company's operating leases for its facilities and finance leases for property and equipment may have both lease components and non-lease components for which the Company has elected to apply the practical expedient to account for each lease component and related non-lease component as one single component. The lease component results in a ROU asset being recorded on the consolidated balance sheets.

For operating leases, lease expense for lease payments is considered operating lease cost and is recognized on a straight-line basis over the lease term. Variable payments for other operating costs, which may be billed based on both usage and as a percentage of the Company's share of total square footage, are considered variable lease cost and are recognized in the period in which the costs are incurred. For finance leases, amortization expense related to finance lease

ROU assets is recognized on a straight-line basis over the earlier of the useful life of the ROU asset or the lease term and interest expense is recognized based on the effective interest method using the Company's incremental borrowing rate. Operating, variable and finance lease cost are recorded as a component of research and development expenses and general and administrative expenses in the consolidated statements of operations and comprehensive loss.

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 and/or optimizing compounds for further development and commercialization, (ii) the transfer of intellectual property rights (licenses), or (iii) options to obtain additional research and development services or licenses for additional intellectual property, upon the payment of option fees.

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 and reimbursement of certain expenses incurred; 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 ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, 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, allocating the transaction price to each performance obligation based on estimated relative standalone selling prices, and measuring progress towards the satisfaction of 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 at contract inception.

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, 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 collaboration partner to develop the intellectual property on their own and whether the required expertise is readily available. In addition, the Company considers whether the customer 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. The initial transaction price of a contract does not include amounts associated with customer option payments.

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 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 contract, the Company recognizes revenue from portion of the transaction price 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 arrangement.

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 customer. 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: A customer's right to choose, at its discretion, to make a payment for additional goods or services is generally considered an option. If the Company is not presently obligated to provide, and does not have a right to consideration for delivering additional goods or services, the item is considered an option. The Company evaluates the customer options for material rights, such as the ability to acquire additional goods or services for free or at a discount. Optional future goods and 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 goods and 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. Milestone payments that may only be achieved after the exercise of a customer option are excluded from the initial determination of the transaction price.

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. Upfront 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.

A change in the scope or price (or both) of a contract is a contract modification if it is approved by the parties and creates new, or changes existing, enforceable rights and obligations of the parties to the contract. The Company accounts for a contract modification as (i) a separate contract if the modification adds distinct goods or services and the price of the contract increases by an amount that reflects the standalone selling price of those additional goods or services; (ii) a termination of the existing contract and creation of a new contract if the remaining goods or services are distinct from those transferred before the modification; (iii) a cumulative catch-up adjustment to the revenue recognized on the original contract if the remaining goods or services are not distinct from those transferred before the modification; or (iv) a combination of (ii) and (iii) if the remaining goods or services include both goods and services that are distinct from those transferred before the modification and goods and services that are not distinct.

For additional information regarding the Company's accounting for collaboration revenue, see Note 9, "Significant agreements."

Research and development costs

Research and development costs are expensed as incurred. Research and development costs consist of costs incurred in performing research and development activities, including salaries, share-based compensation and benefits, travel, facilities costs, depreciation, materials and laboratory supplies, and external costs of outside vendors engaged to conduct preclinical development and clinical development activities, as well as costs to manufacture clinical trial materials. Facilities costs primarily include the allocation of rent and utilities.

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.

Accrued external research and development expenses

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 estimating accrued liabilities, the Company analyzes progress of the research and development and manufacturing activities, including the level of service performed and the associated cost incurred, invoices received and contracted costs. Significant judgments and estimates are made by management in estimating external research and development expenses incurred and associated 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 U.K., receives reimbursements of certain research and development expenditures as part of a U.K. government research and development tax reliefs program. For 2023 and 2024, the Company benefitted from the Small and Medium-sized Enterprises ("SME") R&D Tax Relief program, under which the Company was able to surrender trading losses that arose from qualifying research and development expenses incurred by the Company's subsidiaries in the U.K. for a cash rebate. The Finance Act 2024, which was enacted in February 2024, replaced the legacy research and development expenditure credit and the SME R&D Tax Relief program with a merged research and development expenditure credit scheme ("RDEC") and an enhanced research and development intensive support scheme ("ERIS"). The Finance Act 2024 also introduced certain restrictions, effective for accounting periods beginning on or after April 1, 2024, on the tax relief that can be claimed for expenditures incurred on subcontracted R&D activities or externally provided workers, where such subcontracted activities are not carried out in the U.K. or such workers are not subject to UK payroll taxes. The Finance Act 2024 increased the cash rebate that may be claimed from 18.6% to 26.97% of qualifying expenditure, retroactively applied to qualifying expenditures incurred after April 1, 2023, if the Company qualifies as "R&D intensive" for an accounting period (broadly, a loss-making SME whose relevant R&D expenditure represents, for accounting periods beginning on or after April 1, 2023, 40%, or, for accounting periods beginning on or after April 1, 2024, 30% of its total expenditure for that accounting period). For periods prior to April 1, 2023 the cash rebate was up to 33.35% of qualifying expenditures. The Company qualified as R&D intensive for the years ended December 31, 2025, 2024 and 2023.

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 consolidated statements of operations and comprehensive loss, as the research and development tax credits are not dependent on the Company 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 $34.9 million, $43.1 million and $23.5 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025 and 2024, the Company had research and development incentives receivable of $35.6 million and $35.7 million, 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.

For share-based awards granted to non-employee consultants, the measurement date 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 share unit award is based on the fair value of the Company's 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 shares, the expected share price volatility, the expected term of the award, the risk-free interest rate and expected dividends.

During 2025, the Company began to estimate its volatility based on the historical volatility of the price of its ordinary shares. Prior to 2025, the Company estimated its volatility by using a blend of its share price history for the length of time it had market data for its shares and the historical volatility of similar public companies for the expected term of each grant. 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 or service costs are classified.

Comprehensive loss

Comprehensive loss includes net loss as well as other changes in shareholders' equity 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 ASC Topic 450, *Contingencies*. The Company expenses costs as incurred in relation to such loss contingencies 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 (benefit from) 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

Basic net loss per share is computed by dividing the net loss by the weighted average number of ordinary shares, including non-voting ordinary shares, outstanding for the period. Diluted net loss is computed by adjusting net loss to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net loss per share is computed by dividing the diluted net loss by the weighted average number of ordinary shares, including non-voting ordinary shares, outstanding for the period, including potential dilutive ordinary shares assuming the dilutive effect of ordinary share equivalents. In periods in which the Company reported a net loss, diluted net loss per share is the same as basic net loss per share, since dilutive ordinary shares are not assumed to have been issued if their effect is anti-dilutive.

Recently adopted accounting pronouncements

In December 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2023-09, *Income Taxes (Topic 740) Improvements to Income Tax Disclosures* ("ASU No. 2023-09"), which prescribes standard categories for the components of the effective tax rate reconciliation and requires disclosure of additional information for reconciling items meeting certain quantitative thresholds, requires disclosure of disaggregated income taxes paid, and modifies certain other income tax-related disclosures. ASU No. 2023-09 is effective for annual periods beginning after December 15, 2024 and allows for adoption on a prospective basis, with a retrospective option. The Company adopted ASU No. 2023-09 for the year ended December 31, 2025 on a prospective basis and the required disclosures have been included in Note 10.

Recently issued accounting pronouncements not yet adopted

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement – Reporting Comprehensive Income – Expense Disaggregation Disclosures (Subtopic 220-40)* ("ASU No. 2024-03"), which requires more detailed disclosures about specified categories of expenses included in certain expense captions presented on the face of the consolidated statements of operations and comprehensive loss, including employee compensation, depreciation and amortization. ASU No. 2024-03 is effective for fiscal years beginning after December 15, 2026, and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The amendments may be applied either prospectively to financial statements issued for reporting periods after the effective date of the ASU or retrospectively to all prior periods presented. The Company is currently evaluating the impact of the adoption of ASU No. 2024-03 on its consolidated financial statement disclosures.

In September 2025, the FASB issued ASU No. 2025-06, *Intangibles – Goodwill and Other – Internal-Use Software (Subtopic 350-40): Targeted Improvements to the Accounting for Internal-Use Software* ("ASU No. 2025-06"), which amends certain aspects of the accounting for and disclosure of software costs under ASC Subtopic 350-40, *Internal-Use Software*. The standard is effective for fiscal years beginning after December 15, 2027 and interim periods within fiscal years beginning after December 15, 2027, with early adoption permitted. The amendments may be applied prospectively, retrospectively, or through a modified prospective transition method. The Company is currently evaluating the potential impact of the adoption of ASU No. 2025-06 on its consolidated financial statements.

In December 2025, the FASB issued ASU No. 2025-10, *Government Grants (Topic 832): Accounting for Government Grants Received by Business Entities* ("ASU No. 2025-10"), which establishes authoritative guidance on the recognition, measurement, presentation, and disclosure of government grants. ASU No. 2025-10 is effective for fiscal years beginning after December 15, 2028, including interim periods within those fiscal years, with early adoption permitted. The Company is currently evaluating the impact of adopting ASU No. 2025-10 on its consolidated financial statements and related disclosures.

3. Fair value of financial assets and liabilities

At December 31, 2025 and 2024, the Company had cash equivalents of $364.2 million and $664.9 million, respectively, consisting of money market funds, which are considered Level 1 assets. As of December 31, 2025 and 2024, there were no other assets or liabilities measured at fair value on a recurring basis.

4. Property and equipment, net

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

	December 31, 2025	December 31, 2024
Laboratory equipment	$ 17,564	$ 14,658
Leasehold improvements	12,031	10,903
Finance lease right-of-use assets	1,106	1,033
Computer equipment and software	634	581
Furniture and office equipment	864	1,290
	32,199	28,465
Less: Accumulated depreciation and amortization	(26,178)	(18,949)
	$ 6,021	$ 9,516

Depreciation and amortization expense was $6.4 million, $7.2 million and $6.5 million for the years ended December 31, 2025, 2024 and 2023, respectively. Depreciation and amortization expense for the years ended December 31, 2025, 2024 and 2023 included amortization expense of $0.2 million, $0.1 million and zero, respectively, related to property and equipment obtained under finance leases.

5. Accrued expenses and other current liabilities

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

	December 31, 2025	December 31, 2024
Accrued employee compensation and benefits	$ 17,000	$ 16,272
Accrued external research and development expenses	20,493	14,978
Accrued professional fees	3,969	4,196
Current portion of operating lease liabilities	2,551	5,328
Current portion of finance lease liabilities	205	175
Other	136	297
	$ 44,354	$ 41,246

In August 2025, the Company announced cost reduction initiatives to reduce planned operating costs, primarily through a workforce reduction. As of December 31, 2025, the workforce reduction is substantially completed and the Company recognized aggregate charges for severance and other employee termination benefits of $5.3 million during the year ended December 31, 2025, of which $4.2 million were included in research and development expenses and $1.1 million were included in general and administrative expenses in the Company's consolidated statements of operations and comprehensive loss. Of the charges recognized during the year ended December 31, 2025, $5.0 million represented

cash expenditure for severance and other employee termination benefits paid during the period, and the remaining $0.3 million in unpaid benefits are included in accrued employee compensation and benefits within accrued expenses and other current liabilities in the Company's consolidated balance sheet as of December 31, 2025.

In August 2024, the Company consolidated all discovery research activities to the Company's headquarters in Cambridge, U.K. As a result, during the year ended December 31, 2024, the Company recognized charges of $2.0 million in severance and other one-time termination benefits, which are included in research and development expenses in the Company's consolidated statements of operations and comprehensive loss, of which $1.6 million were paid during the year ended December 31, 2024, and the Company had a remaining liability of $0.4 million related to unpaid severance and other one-time termination benefits included in accrued expenses and other current liabilities in the Company's consolidated balance sheet as of December 31, 2024, all of which was paid during the year ended December 31, 2025.

6. Debt

On September 30, 2020, Bicycle Therapeutics plc and its subsidiaries (the "Borrowers") entered into a loan and security agreement (the "Loan Agreement") with Hercules, as amended from time to time, which provided for aggregate maximum borrowings of up to $75.0 million, of which the Company had drawn down an aggregate of $30.0 million in 2021 and 2020. Payments on borrowings under the Loan Agreement were interest-only until April 1, 2025 and interest was paid at an annual rate of the *Wall Street Journal* prime rate plus 4.55%, with a minimum annual rate of at least 8.05%, capped at a rate no greater than 9.05%, and the Loan Agreement included a 5.0% end-of-term charge payable upon maturity or repayment. The scheduled maturity date was July 1, 2025. On July 9, 2024, the Company repaid all amounts outstanding, including the outstanding borrowings of $30.0 million, accrued and unpaid interest of $0.1 million, an end-of-term charge of $1.5 million and a prepayment charge of $0.3 million, for a total aggregate payment of $31.9 million, and terminated the Loan Agreement. The Company recognized a loss on extinguishment of debt of $1.0 million during the year ended December 31, 2024 in connection with the repayment and termination of the Loan Agreement. Interest expense associated with the Loan Agreement for the years ended December 31, 2025, 2024 and 2023 was zero, $1.6 million and $3.1 million, respectively. Upon termination of the Loan Agreement, all security interests granted to the secured parties thereunder were terminated and released.

7. Ordinary shares

The Company's ordinary shares are divided into two classes: (i) ordinary shares and (ii) non-voting 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. Holders of American Depositary Shares ("ADSs") are not treated as holders of the Company's ordinary shares, unless they withdraw the ordinary shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of the Company's ordinary shares, other than the rights that they have pursuant to the deposit agreement with the depositary.

The non-voting ordinary shares have the same rights and restrictions as the ordinary shares and otherwise rank *pari passu* in all respects with the ordinary shares except for the following:

- a holder of non-voting ordinary shares shall, in relation to the non-voting ordinary shares held, have no right to receive notice of, or to attend or vote at, any general meeting of shareholders save in relation to a variation of class rights of the non-voting ordinary shares;

- the non-voting ordinary shares shall be re-designated as ordinary shares by the Company's board of directors, or a duly authorized committee or representative thereof, upon receipt of a re-designation notice and otherwise subject to the terms and conditions set out in the terms of issue. A holder of non-voting ordinary shares shall not be entitled to have any non-voting ordinary shares re-designated as ordinary shares where such re-designation would result in such holder thereof beneficially owning (for purposes of section 13(d) of the Exchange Act), when aggregated with "affiliates" and "group" members with whom

such holder is required to aggregate beneficial ownership for the purposes of section 13(d) of the Exchange Act, in excess of 9.99% of any class of the Company's securities registered under the Exchange Act (which percentage may be increased or decreased on a holder-by-holder basis subject to the provisions set out in the terms of issue); and

- the non-voting ordinary shares shall be re-designated as ordinary shares automatically upon transfer of a non-voting ordinary share by its holder to any person that is not an "affiliate" or "group" member with whom such holder is required to aggregate beneficial ownership for purposes of section 13(d) of the Exchange Act. This automatic re-designation shall only be in respect of the non-voting ordinary shares that are subject to such transfer.

As of December 31, 2025 and 2024, the Company had not declared any dividends.

As of December 31, 2025 and 2024, the Company's authorized capital share consisted of 159,685,229 and 155,876,645 ordinary shares, respectively, including ordinary shares and non-voting ordinary shares, with a nominal value of £0.01 per share. Authorized share capital, or shares authorized, comprises (i) the currently issued and outstanding ordinary shares and non-voting ordinary shares, (ii) the remaining ordinary shares available for allotment under the existing authority granted to the Board at the annual general meeting held on May 16, 2024, (iii) ordinary shares issuable on the exercise of outstanding options and settlement of vested restricted share units ("RSUs"), and (iv) ordinary shares reserved for issuance under the Bicycle Therapeutics plc 2024 Inducement Plan (the "2024 Inducement Plan"), the Bicycle Therapeutics plc 2020 Equity Incentive Plan (as amended from time to time, the "2020 Plan"), and/or the Bicycle Therapeutics plc 2019 Employee Share Purchase Plan (the "ESPP").

As of December 31, 2025, there were 49,929,952 ordinary shares issued and outstanding and 19,437,944 non-voting ordinary shares issued and outstanding.

8. Share-based compensation

Employee incentive pool

2024 Inducement Plan

In July 2024, the Company's board of directors approved the 2024 Inducement Plan. The 2024 Inducement Plan allows for the granting of nonqualified share options, RSUs, and other equity awards under the plan to persons not previously an employee or director of the Company, or following a bona fide period of non-employment, as an inducement material to such persons entering into employment with the Company. Share options granted under the 2024 Inducement Plan have a 10-year contractual life and generally vest over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date and the balance thereafter in 36 equal monthly installments. In the event of a Change in Control of the Company, as defined in the 2024 Inducement Plan, any outstanding awards under the 2024 Inducement Plan will vest in full immediately prior to such change of control.

The Company initially reserved 1,500,000 of its ordinary shares, or the equivalent number of ADSs, for the issuance of awards under the 2024 Inducement Plan. As of December 31, 2025, there were 925,581 shares available for future issuance under the 2024 Inducement Plan.

As of December 31, 2025, there were options to purchase 574,419 shares outstanding under the 2024 Inducement Plan.

2020 Equity Incentive Plan

In June 2020, the Company's shareholders first approved the 2020 Plan, under which the Company may grant market value options, market value stock appreciation rights or restricted shares, RSUs, performance RSUs and other share-based awards to the Company's employees. The Company's non-employee directors and consultants are eligible to receive awards under the 2020 Non-Employee Sub-Plan to the 2020 Plan. All awards under the 2020 Plan, including the

2020 Non-Employee Sub-Plan, will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms, change of control provisions and post-termination exercise limitations. In the event of a change of control of the Company, as defined in the 2020 Plan, any outstanding awards under the 2020 Plan will vest in full immediately prior to such change of control.

The ordinary shares reserved for future issuance under the 2020 Plan includes shares subject to options that were granted under the Company's 2019 Share Option Plan (the "2019 Plan") and that were granted pursuant to option contracts granted prior to the Company's IPO, in each case that expire, terminate, are forfeited or otherwise not issued from time to time, if any. Prior to June 2025, the number of ordinary shares reserved for issuance pursuant to the 2020 Plan automatically increased on the first day of January of each year, initially commencing on January 1, 2021 and continuing up to and including January 1, 2032, in an amount equal to 5% of the total number of the Company's voting 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 (the "Evergreen Increase"). In June 2025, the Company's shareholders approved Amendment No. 1 to the 2020 Plan which (i) amended the calculation of the Evergreen Increase to capture the Company's total issued share capital in order to treat non-voting ordinary shares the same as voting ordinary shares, and (ii) increased the number of ordinary shares reserved for future issuance by 1,300,000. As of December 31, 2025, there were 2,178,641 shares available for issuance under the 2020 Plan. The number of shares reserved for issuance under the 2020 Plan was increased by 3,468,394 shares effective January 1, 2026.

Share options granted under the 2020 Plan have a 10-year contractual life, and generally vest over either a three-year service period in three equal annual installments for new non-employee director grants, or a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date and the balance thereafter in 36 equal monthly installments for employees and consultants. Certain options granted to the Company's non-employee directors vest over a one-year service period in four equal quarterly installments.

The Company grants RSUs to non-employee directors, consultants and certain employees under the 2020 Plan. Each RSU represents the right to receive one of the Company's ordinary shares upon vesting. RSUs granted to employees and consultants vest over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date and the remaining RSUs vesting in 12 equal quarterly installments. Certain RSUs granted to the Company's non-employee directors either vest over a three-year service period in three equal annual installments for new non-employee director grants or over a one-year service period in four equal quarterly installments. The Company may also, in its sole discretion, provide for deferred settlement of RSUs granted to the Company's non-employee directors.

As of December 31, 2025, there were options to purchase 7,024,208 shares and RSUs for 1,644,421 shares outstanding under the 2020 Plan.

2019 Share Option Plan

In May 2019, the Company adopted the 2019 Plan, which became effective in conjunction with the IPO. As of December 31, 2025, there were 1,699,408 options to purchase ordinary shares outstanding under the 2019 Plan. In conjunction with the adoption of the 2020 Plan, all shares available for future issuance under the 2019 Plan as of June 29, 2020 became available for issuance under the 2020 Plan and the Company ceased making awards under the 2019 Plan. The 2020 Plan is the successor of the 2019 Plan.

Share options previously issued under the 2019 Plan have a 10-year contractual life, and generally 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. Certain awards granted to the Company's non-employee directors were fully vested on the date of grant. The exercise price of share options issued under the 2019 Plan is not less than the fair value of ordinary shares as of the date of grant.

Employee Share Purchase Plan ("ESPP")

In May 2019, the Company adopted the ESPP, which became effective in conjunction with the IPO. The Company initially reserved 215,000 ordinary shares for future issuance under this plan. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020 and each January 1 thereafter through January 1, 2029, by the lower of (i) 1% of the outstanding number of ordinary shares on the immediately preceding December 31; (ii) 430,000 ordinary shares or (iii) such lesser number of shares as determined by the Compensation Committee. The number of shares reserved under the ESPP is subject to adjustment in the event of a split-up, share dividend or other change in the Company's capitalization. As of December 31, 2025, the total number of shares available for issuance under the ESPP was 2,007,671 shares. The number of shares reserved for issuance under the ESPP was increased by 430,000 shares effective January 1, 2026. As of December 31, 2025, 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,		
	2025	2024	2023
Research and development expenses	$ 18,024	$ 19,424	$ 15,581
General and administrative expenses	21,440	18,657	16,896
	$ 39,464	$ 38,081	$ 32,477

Share options

The following table summarizes the Company's option activity since December 31, 2024:

	Number of Shares Underlying Share Options	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2024	8,748,726	$ 22.41	6.81	$ 9,559
Granted	1,916,838	12.38	—	—
Exercised	(10,116)	3.39	—	—
Forfeited	(852,342)	23.21	—	—
Outstanding as of December 31, 2025	9,803,106	$ 20.40	6.22	$ 2,680
Vested and expected to vest as of December 31, 2025	9,803,106	$ 20.40	6.22	$ 2,680
Options exercisable as of December 31, 2025	6,640,966	$ 22.17	5.11	$ 2,670

The weighted average grant-date fair value of share options granted during the years ended December 31, 2025, 2024 and 2023 was $8.47 per share, $13.52 per share and $19.36 per share, respectively.

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, 2025, 2024 and 2023 was $0.1 million, $5.1 million and $0.5 million, respectively.

For the years ended December 31, 2025, 2024 and 2023, the Company recorded share-based compensation expense for share options granted of $28.2 million, $30.2 million and $27.0 million, respectively.

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,		
	2025	2024	2023
Risk-free interest rate	4.3 %	4.0 %	4.0 %
Expected volatility	74.0 %	77.0 %	82.9 %
Expected dividend yield	—	—	—
Expected term (in years)	6.1	6.1	6.1

As of December 31, 2025, total unrecognized compensation expense related to the share options was $29.3 million, which is expected to be recognized over a weighted average period of 2.2 years.

Restricted share units

The following table summarizes the Company's RSU activity under the 2020 Plan since December 31, 2024:

	Number of Shares Underlying RSUs	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2024	674,262	$ 22.96
Granted	1,452,927	13.74
Vested and settled	(296,362)	25.03
Vested and deferred[(1)]	(55,293)	15.17
Forfeited	(228,406)	14.77
Unvested outstanding at December 31, 2025	1,547,128	15.40
Vested but subject to deferred settlement at December 31, 2024[(1)]	42,000	18.07
Vested and deferred[(1)]	55,293	15.17
Vested but subject to deferred settlement at December 31, 2025[(1)]	97,293	16.42
Outstanding at December 31, 2025	1,644,421	$ 15.46

(1) The Company granted certain RSUs to the Company's non-employee directors which provided for deferred settlement of the RSUs to a specified date following the first to occur of (i) the date of the director's separation from service, (ii) the date of the director's disability, (iii) the date of the director's death or (iv) the date of a change in control event.

The fair value of RSUs that vested during the years ended December 31, 2025, 2024 and 2023 was $3.7 million, $3.8 million and $3.0 million, respectively.

Total share-based compensation expense for RSUs granted for the years ended December 31, 2025, 2024 and 2023 was $11.3 million, $7.9 million and $5.5 million, respectively. As of December 31, 2025, the total unrecognized compensation expense related to RSUs was $16.8 million, which is expected to be recognized over a weighted-average period of 2.6 years.

9. Significant agreements

The following table summarizes the revenue recognized from the Company's collaboration arrangements in the consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Collaboration revenue			
Bayer	$ 8,920	$ 3,393	$ 1,160
Novartis	46,985	8,161	1,909
Ionis	2,000	8,881	10,734
Genentech	14,681	14,840	11,969
AstraZeneca	—	—	1,204
Total collaboration revenue	$ 72,586	$ 35,275	$ 26,976

Bayer Collaboration Agreement

On May 4, 2023, the Company and Bayer entered into a collaboration and license agreement (the "Bayer Collaboration Agreement"), pursuant to which the parties will perform research and discovery activities under a mutually agreed upon research plan during a research term up to a specified number of years per target program to generate radiopharmaceutical compounds incorporating optimized Bicycle constructs directed to two specified targets. Bayer also has a one-time right to expand the collaboration to include a third target program, and with respect to each of the up to three target programs, Bayer has an option, exercisable within a specified period of time following the effective date of the Bayer Collaboration Agreement, to generate, develop and commercialize non-radiopharmaceutical compounds directed to the applicable target, either itself or in collaboration with the Company. Bayer also has certain limited target substitution rights, in certain cases subject to specified additional payments.

For each collaboration program, Bayer may elect, at its sole discretion, to progress compounds arising from research activities into further preclinical development of potential products directed to the target of such collaboration program. On a target-by-target basis, if Bayer elects to progress development candidates directed to such target into further clinical development, Bayer will be responsible for all future development, manufacturing, and commercialization activities and be required to use commercially reasonable efforts to develop and seek regulatory approval in certain major markets for products directed to the applicable target.

Bayer paid an upfront payment to the Company of $45.0 million in July 2023. All other payments under the Bayer Collaboration Agreement will be made in British Pound Sterling. If Bayer elects to expand the collaboration to include an additional target program, it will be required to make a one-time payment to the Company in the high single-digit millions. In addition, on a target-by-target basis, if Bayer elects to exercise its option to expand its rights with respect to such target to develop and commercialize non-radiopharmaceutical compounds directed to such target, Bayer will be required to pay to the Company either a one-time option fee payment or quarterly payments of specified installment amounts for a specified maximum time period during which the Company is performing research activities, with the aggregate amounts receivable by the Company ranging from the high single-digit millions in the case of the one-time option fee payment, to the low single-digit millions in the case of the quarterly installments, in each case where the Company is performing specified research activities following the exercise of the option. Additionally, for each collaboration program, Bayer will reimburse the Company for certain expenses incurred in connection with specified research and discovery activities performed by a contract research organization ("CRO").

On a target-by-target basis for the up to three targets, if Bayer elects to progress one or more candidate compounds into further development, Bayer will be required to pay a candidate selection fee for the first such compound progressed by Bayer directed to such target that incorporates a radionuclide, and for the first such compound directed to such target that does not incorporate a radionuclide (and for which Bayer has not paid the one-time option fee payment for non-radiopharmaceutical compounds), ranging from high single-digit millions to the mid single-digit millions. On a

target-by-target basis, if Bayer successfully conducts clinical development and achieves regulatory approval for compounds arising from the collaboration directed to such target in two indications, Bayer will be required to pay to the Company development and regulatory/first commercial sale milestones of up to £178.3 million for the first product directed to the applicable target to achieve such milestones, or £534.9 million across all three potential target programs. In addition, if Bayer successfully commercializes products arising from the collaboration, Bayer will be required to pay to the Company, on a product-by-product basis, tiered royalties on net sales of products by Bayer, its affiliates or sublicensees at percentages ranging from the mid-single digits to the very low double digits, subject to standard reductions and offsets in certain circumstances, and a royalty floor. If Bayer commercializes diagnostic products directed to a target, royalties will be payable on such diagnostic products at a specified reduced percentage of the rates for therapeutic products. Royalties will be payable under the Bayer Collaboration Agreement on a product-by-product and country-by-country basis, commencing on the first commercial sale of each product, until the latest of (a) the expiration of the last valid claim of certain patents licensed by the Company to Bayer, (b) a specified number of years following first commercial sale of such product, and (c) expiration of all data and regulatory exclusivity for such product in the applicable country. On a target-by-target basis, Bayer will also owe the Company tiered sales milestones based on the achievement of specified levels of net sales of therapeutic products directed to such target totaling up to £194.5 million in the aggregate per target, or £583.5 million across all three potential target programs, and on diagnostic products directed to such target at a low double digit percentage of the therapeutic product milestones.

The closing of the Bayer Collaboration Agreement was subject to the clearance of the transaction under the U.K. National Security and Investment Act 2021, which occurred on June 22, 2023.

The Company identified the following performance obligations at inception of the arrangement: (i) two combined performance obligations each comprised of a license and related research and development services during the research term associated with radiopharmaceutical compounds for each of the initial targets; (ii) a material right associated with certain limited substitution rights with respect to either of the initial targets; (iii) two material rights associated with the option to progress radiopharmaceutical candidates directed to each of the initial targets into further development; (iv) two material rights associated with the options to generate, develop, and commercialize non-radiopharmaceutical compounds for each of the initial targets, for which each option includes an underlying option for research and development services and an option to progress non-radiopharmaceutical candidates directed to the first and second targets into further development; and (v) a material right related to the option to expand the collaboration to include a third target, which upon exercise includes research and development services during the research term associated with radiopharmaceutical compounds directed to the third target, as well as underlying options for certain limited substitution rights; an option to progress a radiopharmaceutical candidate directed to the third target into further development; and an option to generate, develop, and commercialize non-radiopharmaceutical compounds directed to the third target, inclusive of an underlying option for research and development services and an option to progress a non-radiopharmaceutical candidate into further development.

The Company concluded that the licenses granted at contract inception are not distinct from the research and development services as Bayer cannot obtain the benefit of the licenses without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as they relate to constrained peptide technology that is not available in the marketplace. As a result, for each target, the license has been combined with the research and development services into a single performance obligation. In assessing whether the various options under the arrangement represent material rights, the Company considered the additional consideration the Company would be entitled to upon option exercise and the standalone selling price of the underlying goods and services. For the material rights identified above, the Company concluded that each of the options provided Bayer with a discount that it otherwise would not have received. The Company exercised judgment in concluding that certain development and commercialization rights associated with progressing product candidates into further development and commercialization represent options that are material rights, as Bayer cannot benefit from the development and commercialization rights until Bayer, in its sole discretion, elects to progress candidates into further development and pays the associated candidate selection fees.

The transaction price was initially determined to be $47.5 million, consisting of the $45.0 million upfront fee and an estimated $2.5 million for the reimbursement of certain external CRO costs. Additional payments to the Company upon Bayer’s exercise of options are excluded from the transaction price as they relate to option fees and

milestones that can only be achieved subsequent to the exercise of an option. The estimated $2.5 million in variable consideration was first allocated entirely to the first and second target combined performance obligations and the remaining 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 combined performance obligations for the initial targets were 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. The estimated standalone selling prices for the material rights were determined based on the fees that Bayer would pay to exercise the options, the estimated value of the underlying goods and services, and the probability that Bayer would exercise the options, inclusive of the probability of technical success.

The Company recognizes revenue related to amounts allocated to the initial target combined performance obligations as the underlying services are performed using a proportional performance model over the period of service using input-based measurements of full-time equivalent efforts and external costs incurred to date as a percentage of total estimated full-time equivalent efforts and external costs, which best reflects the progress towards satisfaction of the performance obligations. The amounts allocated to the material rights are recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the respective option.

In November 2025, Bayer provided the Company with a notice of termination of one of the initial target programs, effective in January 2026. The Company accounted for the notice of termination as a contract modification in the fourth quarter of 2025 as the notice of termination reduced the scope of the arrangement. As a result, the Company allocated the remaining unrecognized transaction price as of the modification date to the remaining unsatisfied and partially satisfied performance obligations and updated the measure of progress as of the modification date, resulting in the recognition of revenue of $5.5 million. The following table summarizes the allocation of the remaining unrecognized transaction price to the remaining unsatisfied and partially satisfied performance obligations as of the modification date (in thousands):

Performance Obligations	Allocation
Combined performance obligation related to the licenses and research and development services associated with radiopharmaceutical compounds directed to the remaining initial target	$ 10,125
Material right associated with limited substitution rights for the remaining initial target	2,206
Material right associated with the option to progress radiopharmaceutical candidates directed to the remaining initial target into further development	10,614
Material right associated with the option to progress a non-radiopharmaceutical compound directed to the remaining initial target	6,288
Material right for the option to expand the collaboration to include an additional target and the underlying additional option rights	10,986
	$ 40,219

The combined performance obligation is expected to be satisfied over approximately the next two years and the remaining material rights are expected to be exercised or expire within approximately seven years from contract inception.

During the years ended December 31, 2025, 2024 and 2023, the Company recognized revenue of $8.9 million, $3.4 million and $1.2 million, respectively, in connection with the Bayer Collaboration Agreement. As of December 31, 2025 and 2024, the Company recorded deferred revenue of $34.6 million and $40.0 million, respectively, in connection with the Bayer Collaboration Agreement.

Novartis Collaboration Agreement

On March 27, 2023, the Company and Novartis entered into a collaboration and license agreement (the "Novartis Collaboration Agreement"), pursuant to which the parties agreed to perform research and discovery activities during a research term of up to a specified number of years per target program to generate compounds incorporating optimized Bicycle constructs directed to two specified targets. The Company granted Novartis a non-exclusive, worldwide, royalty-free, sublicensable (subject to certain restrictions) license under the Company's intellectual property

solely for Novartis to perform its research activities for each collaboration program during the research term (the "Novartis Research License"). For each collaboration program, Novartis could elect to progress compounds arising from activities under the research programs ("Licensed Compounds") into further preclinical development and at a specified point the Company would grant Novartis an exclusive, royalty-bearing, sublicensable, license under certain of the Company's intellectual property to develop, manufacture, and commercialize such Licensed Compound, subject to certain limitations. Novartis also had certain limited substitution rights for each target. On a target-by-target basis, if Novartis elected to progress development candidates directed to such target into further development, Novartis would have been responsible for all future development, manufacturing and commercialization activities and be required to use commercially reasonable efforts to develop and seek regulatory approval in certain major markets for products containing Licensed Compounds directed to the applicable target.

Novartis paid a nonrefundable upfront payment to the Company of $50.0 million in April 2023. During the research term, upon achievement of a specified discovery milestone for the first target program, Novartis was required to make a one-time payment to the Company in the low single digit millions. On a target-by-target basis, if Novartis elected to progress one or more candidate compounds into further development and obtain an exclusive license for commercialization, Novartis would be required to pay a candidate selection fee for the first such Licensed Compound progressed by Novartis that incorporates a radionuclide, and for the first such Licensed Compound that does not incorporate a radionuclide, in each case in the mid-teen millions.

The Company identified the following performance obligations at the inception of the arrangement: (i) two combined performance obligations each comprised of the Novartis Research License and the related research and development services during the research term for each target; (ii) two material rights associated with limited substitution rights with respect to each target; (iii) two material rights associated with the options to progress development candidates that incorporate a radionuclide with respect to each target; and (iv) two material rights associated with the option to progress development candidates that do not incorporate a radionuclide with respect to each target. The Company concluded that the Novartis Research License was not distinct from the research and development services as Novartis could not obtain the benefit of the licenses without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as they relate to constrained peptide technology that is not available in the marketplace. As a result, for each target, the Novartis Research License was combined with the research and development services into a single performance obligation. In assessing whether the various options under the agreement represent material rights, the Company considered the additional consideration the Company would have been entitled to upon option exercise and the standalone selling price of the underlying goods and services. For the material rights identified above the Company concluded that each of the options provided Novartis with a discount that it otherwise would not have received.

The total transaction price was initially determined to be $50.0 million, consisting of the $50.0 million upfront fee. Variable consideration for certain development milestones not subject to option exercises was fully constrained at inception as a result of the uncertainty regarding whether any of the milestones would be achieved. Additional consideration to be paid to the Company upon the exercise of options by Novartis was excluded from the transaction price as they relate to certain option fees, milestones and royalties that can only be achieved subsequent to the exercise options. In November 2024, the Company achieved the specified discovery milestone for the first target program and updated its estimate of the variable consideration to include an additional $3.0 million that was no longer constrained. As a result, the transaction price increased to $53.0 million.

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 combined performance obligations for each of the targets were 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 for what would be expected to be realized under similar contracts. The estimated standalone selling prices for the material rights were determined based on the fees Novartis would pay to exercise the options, the estimated value of the underlying goods and services, and the probability that Novartis would exercise the options, inclusive of the probability of technical success.

The Company recognized revenue related to amounts allocated to the combined performance 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 efforts and external costs incurred to date as a percentage of total estimated full-time equivalent efforts and external costs, which best reflected the progress towards satisfaction of the performance obligations. The amounts allocated to the material rights were recorded as deferred revenue and the Company would commence revenue recognition upon exercise of or upon expiry of the respective option. During the year ended December 31, 2024, the Company recognized revenue of $2.5 million upon the expiration of Novartis' material rights for limited substitution rights for each target.

In November 2025, Novartis provided the Company with a notice of termination of the Novartis Collaboration Agreement in its entirety, effective in February 2026 after a contractual 90-day notice period. Management exercised significant judgment in concluding that the notice of termination should be accounted for as a contract modification in the fourth quarter of 2025, as the notice of termination reduces the scope of the arrangement. Management concluded that the notice of termination substantively removes all remaining performance obligations, including remaining material rights, as of the date of the notice as Novartis will not benefit from any remaining activities performed during the notice period and the likelihood of exercising any remaining options is remote. As a result, the Company recognized the remaining unrecognized transaction price of $41.9 million as revenue on the date of the notice of termination.

During the years ended December 31, 2025, 2024 and 2023, the Company recognized revenue of $47.0 million, $8.2 million and $1.9 million in connection with the Novartis Collaboration Agreement. As of December 31, 2025 and 2024, the Company recorded deferred revenue of zero and $44.1 million, respectively, in connection with the Novartis Collaboration Agreement.

Ionis Agreements

On July 9, 2021, following the exercise by Ionis of an option granted pursuant to an evaluation and option agreement, the Company and Ionis entered into a collaboration and license agreement (as amended, the "Ionis Collaboration Agreement"). Pursuant to the Ionis Collaboration Agreement, the Company granted to Ionis a worldwide exclusive license under the Company's relevant technology to research, develop, manufacture and commercialize products incorporating Bicycle peptides directed to the protein coded by the gene TFRC1 (transferrin receptor) ("TfR1 Bicycle" molecules) intended for the delivery of oligonucleotide compounds directed to targets selected by Ionis for diagnostic, therapeutic, prophylactic and preventative uses in humans. Ionis will maintain exclusivity to all available targets unless it fails to achieve specified development diligence milestone deadlines. If Ionis fails to achieve one or more development diligence milestone deadlines, the Company has the right to limit exclusivity to certain specific collaboration targets, subject to the payment by Ionis of a low single-digit million dollar amount per target as specified in the Ionis Collaboration Agreement. Each party was responsible for optimization of such TfR1 Bicycle molecules and other research and discovery activities related to TfR1 Bicycle molecules, as specified by a research plan, under which the Company performed research and discovery activities including a baseline level of effort for a period of three years. The research plan substantially completed in the second quarter of 2024. Ionis is responsible for all future research, development, manufacture and commercialization activities. The Company has retained certain rights, including the right to use TfR1 Bicycle molecules for all non-oligonucleotide therapeutic purposes.

Under the Ionis Collaboration Agreement, Ionis made a non-refundable upfront payment of $31.0 million in addition to $3.0 million already paid under an evaluation and option agreement, and reimbursed the Company for certain pass-through costs incurred. If Ionis is at risk of failing to achieve a specified development diligence milestone deadline, it can make up to three separate payments of a mid-single-digit million dollar amount to extend the development diligence milestone deadlines. On a collaboration target-by-collaboration target basis, Ionis will be required to make a low single-digit million dollar payment upon acceptance of an investigational new drug application ("IND") for the first product directed to such collaboration target (provided that Ionis will have a high single-digit million dollar credit to be applied towards the IND acceptance fee for four collaboration targets, or for exclusivity payments for certain targets if specified development diligence milestones deadlines are not achieved), and Ionis will be required to make milestone payments upon the achievement of specified development and regulatory milestones of up to a low double-digit million dollar amount per collaboration target. In addition, the Company is eligible to receive up to a low double-digit million dollar amount in cumulative sales milestone payments. The Company is also entitled to receive tiered royalty payments on net sales at percentages in the low single-digits, subject to certain standard reductions and offsets. Royalties will be payable, on a product-by-product and country-by-country basis, until the latest of the expiration of specified licensed

patents covering such product in such country, ten years from first commercial sale of such product in such country, or expiration of marketing exclusivity for such product in such country.

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

Concurrently with the execution of the Ionis Collaboration Agreement on July 9, 2021, the Company entered into a share purchase agreement (the "Ionis Share Purchase Agreement") with Ionis, pursuant to which Ionis purchased 282,485 of the Company's ordinary shares (the "Ionis Shares") at a price per share of $38.94, for an aggregate purchase price of approximately $11.0 million. The Company determined the fair value of the Ionis Shares to be $7.6 million, based on the closing price of the Company's ADSs of $31.11 per ADS on the date of the Ionis Share Purchase Agreement, less a discount for lack of marketability associated with certain resale restrictions applicable to the Ionis Shares. The Company concluded that the premium paid by Ionis under the Ionis Share Purchase Agreement represents additional consideration for the goods and services to be provided under the Ionis Collaboration Agreement and as such, the total premium of $3.4 million was included in the transaction price under the Ionis Collaboration Agreement.

The Company identified the following performance obligations at the inception of the arrangement: (i) a combined performance obligation comprised of the worldwide exclusive license to research, develop, manufacture and commercialize products incorporating TfR1 Bicycle molecules under the arrangement and the research and discovery activities to customize and optimize such TfR1 Bicycle molecules; and (ii) four material rights associated with options to obtain credits to be applied towards the IND acceptance fee for four collaboration targets. The Company concluded that the exclusive license to research, develop, manufacture and commercialize products was not distinct from the research and discovery services as Ionis could not benefit from the license without the Company performing the research and discovery services. The services incorporated proprietary technology, unique skills and specialized expertise to optimize Bicycle molecules that were not available in the marketplace, and therefore the license was combined with the research and discovery activities into a single performance obligation. The Company concluded that the low-single-digit million dollar payments upon acceptance of an IND is a customer option, as Ionis has the contractual right to choose to make the payment in exchange for the continued exclusive right to research, develop, manufacture and commercialize the product candidate, and the Company is not presently obligated to provide, and does not have a right to consideration, for the additional goods or services prior to Ionis's exercise of the option. In assessing whether the options under the Ionis Collaboration Agreement represent material rights, the Company considered the additional consideration the Company would be entitled to upon the option exercise and the standalone selling price of the underlying goods and services. For the material rights identified as performance obligations above, the Company concluded that each of the options to obtain credits provided Ionis with a discount that it otherwise would not have received without entering into the Ionis Collaboration Agreement.

The total transaction price was initially determined to be $38.0 million, consisting of the $31.0 million up front payment, the $3.0 million payment under the evaluation and option agreement, the $3.4 million premium paid under the Ionis Share Purchase Agreement, and an estimated $0.6 million for the reimbursement of CRO costs. Additional variable consideration including development diligence milestone deadline extension payments, development and regulatory milestone payments, sales milestone payments and royalty payments was fully constrained as a result of the uncertainty regarding whether any of the milestones will be achieved. During the year ended December 31, 2024, the Company updated its estimate of variable consideration for the reimbursement of CRO costs from $0.6 million to $0.4 million, and the transaction price decreased to $37.8 million.

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 price of the combined licenses and research and discovery performance obligation was based on the nature of the licenses to be delivered, as well as the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit

margin. The estimated standalone selling price for the material rights was determined based on the estimated value of the underlying goods and services, and the probability that Ionis would exercise the option.

The Company recognized revenue related to amounts allocated to the combined licenses and research and discovery performance obligation using a proportional performance model over the period of service using input-based measurements including total full-time equivalent effort and CRO costs incurred to date as a percentage of total estimated full-time equivalent effort and CRO costs, which best reflects the progress towards satisfaction of the performance obligation. The combined licenses and research and discovery performance obligation was fully satisfied in the second quarter of 2024. In July 2025, an investigational medicine incorporating a TfR1 Bicycle molecule under the Ionis Collaboration Agreement achieved acceptance of an investigational new drug application ("IND") upon which Ionis paid the Company $2.0 million. As a result, the transaction price increased from $37.8 million to $39.8 million, and the Company recognized revenue of $2.0 million during the year ended December 31, 2025.

The remaining amount of the transaction price allocated to material rights is recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the respective option. The Company anticipates the material rights may be exercisable or may expire within seven years from contract execution.

In December 2021 and April 2023, the Company entered into amendments to the Ionis Collaboration Agreement to perform additional research services and Ionis paid the Company $1.6 million and $0.8 million, respectively. The Company concluded that the December 2021 amendment was a separate contract, which was modified by the April 2023 amendment. Revenue was recognized using a proportional performance model over the period of service using input-based measurements of total full time equivalent efforts and external costs incurred to date as a percentage of total expected full time equivalent efforts and expected external costs, which best reflects the progress towards satisfaction of the performance obligation. All revenue from the amendments has been recognized as of December 31, 2025.

For the years ended December 31, 2025, 2024 and 2023, the Company recognized $2.0 million, $8.9 million and $10.7 million in revenue, respectively, and as of December 31, 2025 and 2024, the Company recorded deferred revenue of $3.8 million and $3.6 million, respectively, in connection with the Ionis Collaboration Agreement.

Genentech Collaboration Agreement

On February 21, 2020, the Company entered into a Discovery Collaboration and License Agreement, as amended from time to time (as amended, the "Genentech Collaboration Agreement"), with Genentech. The collaboration was 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 (each a "Genentech Collaboration Program") suitable for Genentech to advance into further development and commercialization.

Under the terms of the Genentech Collaboration Agreement, the Company received a $30.0 million upfront, non-refundable payment. The initial discovery and optimization activities were focused on utilizing the Company's phage screening technology to identify product candidates aimed at two immuno-oncology targets ("Genentech Collaboration Programs #1 and #2"), which may have also included additional discovery and optimization of Bicycle molecules as a targeting element for each Genentech Collaboration Program (each a "Targeting Arm"). Genentech also had the option to nominate up to two additional immuno-oncology targets (each, an "Expansion Option") as additional Genentech Collaboration Programs, which may have also included an additional Targeting Arm for each Expansion Option. Genentech exercised the Expansion Options in October 2021 and June 2022 ("Genentech Collaboration Programs #3 and #4"), respectively and paid to the Company an expansion fee of $10.0 million for each Expansion Option.

The Company granted to Genentech a non-exclusive research license under the Company's intellectual property solely to enable Genentech to perform any activities under the agreement. If the Company performed the initial discovery and optimization activities in accordance with an agreed upon research plan and achieved specified criteria, Genentech had the option to have the Company perform initial pre-clinical development and optimization activities in

exchange for an additional specified milestone payment in the mid-single digit millions for each Genentech Collaboration Program (the "LSR Go Option"). Upon completion of such initial pre-clinical development and optimization activities for each Genentech Collaboration Program, Genentech had the option to obtain an exclusive license to exploit any compound developed under such Genentech Collaboration Program in exchange for an additional specified payment in the mid to high single digit millions for each of Genentech Collaboration Programs #1 through #4 (the "Dev Go Option").

The Company identified the following performance obligations at inception of the arrangement: (i) a combined performance obligation comprised of the research license and the related research and development services through LSR Go for Genentech Collaboration Program #1; (ii) a combined performance obligation comprised of the research license and the related research and development services through LSR Go for Genentech Collaboration Program #2; (iii) a material right associated with an option to a specified Targeting Arm for Genentech Collaboration Program #1; (iv) two material rights associated with the LSR Go Option for Genentech Collaboration Program #1 and Genentech Collaboration Program #2, which includes research services to be provided through the Dev Go Option; (v) material rights associated with certain limited substitution rights with respect to a limited number of collaboration targets; and (vi) two material rights related to each Genentech Expansion Option, which upon exercise included the services for an additional immuno-oncology target through LSR Go, an LSR Go Option which includes the services to be provided through the Dev Go Option, limited substitution rights, and an option to select a specified Targeting Arm.

The Company concluded that the research license was not distinct from the research and development services as Genentech could not 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 program, the research license was combined with the research and development services into a single performance obligation. In addition, the Company concluded that the Dev Go Option was not distinct or separately exercisable from the LSR Go Option, as the customer could not benefit from the Dev Go Option unless and until the LSR Go Option was exercised.

In assessing whether the various options under the Genentech Collaboration Agreement represented material rights, the Company considered the additional consideration the Company would be entitled to upon the option exercise, the standalone selling price of the underlying goods, services, and additional options. For the material rights identified above the Company concluded that each of the options provided Genentech with a discount that it otherwise would not have received.

The total transaction price was initially determined to be $31.0 million, consisting of the $30.0 million upfront fee and an additional $1.0 million for Genentech's selection of a new Targeting Arm associated with Genentech Collaboration Program #2 at inception. Additional consideration to be paid to the Company upon the exercise of options by Genentech and subsequent milestones were excluded from the transaction price as they relate to option fees and milestones that could only be achieved subsequent to the exercise of an option. In addition, other variable consideration for development milestones not subject to option exercises was fully constrained, as a result of the uncertainty regarding whether any of the milestones would be achieved. In March 2021, the transaction price was increased to $33.0 million as a result of the Company's achievement of specified criteria for the Targeting Arm associated with Genentech Collaboration #2.

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 Genentech Collaboration Programs was 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. The estimated standalone selling price for the material rights was determined based on the fees Genentech would pay to exercise the options, the estimated value of the underlying goods and services, and the probability that Genentech would exercise the option and any underlying options.

In October 2021 and June 2022, respectively, Genentech exercised the first and second Expansion Options to add Genentech Collaboration Programs #3 and #4 and paid to the Company an expansion fee of $10.0 million each. For Genentech Collaboration Program #3, Genentech also elected for the Company to perform discovery and optimization

services for a Targeting Arm, and the Company received an additional payment of $1.0 million. The Company concluded that the exercise of each Expansion Option, including the option to a specified Targeting Arm for Genentech Collaboration Program #3, is accounted for as a continuation of the existing contract as the customer decided to purchase additional goods and services contemplated in the original contract. The additional arrangement consideration for each Expansion Option as well as the amounts originally allocated to each Expansion Option were allocated to the underlying goods and services associated with each Expansion Option on the same basis as the initial allocation of the Genentech Collaboration Agreement. In December 2022 upon achievement of specified criteria for the Targeting Arm associated with Genentech Collaboration Program #3, the Company allocated the additional consideration received of $2.0 million entirely to the Genentech Collaboration Program #3 and Targeting Arm services as the terms of the variable consideration relate specifically to the Company's efforts in satisfying the performance obligation and allocating the variable consideration entirely to the performance obligation is consistent with the allocation objective in ASC 606. Other variable consideration for development milestones not subject to option exercises was fully constrained as a result of the uncertainty regarding whether any of the milestones will be achieved.

The Company recognized revenue related to amounts allocated to the Genentech Collaboration Program #1 through #4 Performance 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 efforts and external costs incurred to date as a percentage of total full-time equivalent efforts and expected external costs, which best reflects the progress towards satisfaction of the performance obligation. The amounts allocated to the material rights were recorded as deferred revenue and the Company would commence revenue recognition upon exercise of or upon expiry of each respective option.

In June 2023, Genentech terminated Genentech Collaboration Program #2 and revenue of $6.0 million was recognized during the year ended December 31, 2023. In January 2024, the JRC decided to discontinue research activities associated with Genentech Collaboration Program #3 and, as a result, the Company recognized revenue of $10.4 million during the year ended December 31, 2024. In January 2025, Genentech provided the Company with a notice of termination for Genentech Collaboration Program #4, effective in March 2025, and the Company recognized revenue of $7.5 million during the year ended December 31, 2025. In July 2025, Genentech provided the Company with a notice of termination of the Genentech Collaboration Agreement, effective in August 2025, and as a result, the Company recognized the remaining deferred revenue under the arrangement of $6.5 million during the year ended December 31, 2025.

For the years ended December 31, 2025, 2024 and 2023, the Company recognized revenue of $14.7 million, $14.8 million and $12.0 million, respectively, and as of December 31, 2025 and 2024, the Company recorded deferred revenue of zero and $14.0 million, respectively, in connection with the Genentech Collaboration Agreement.

Summary of Contract Assets and Liabilities

The following table presents changes in the balances of the Company's contract liabilities (in thousands):

	Beginning Balance January 1, 2025	Additions	Deductions	Impact of Exchange Rates	Ending Balance December 31, 2025
Contract liabilities:					
Deferred revenue					
Bayer collaboration deferred revenue	$ 39,960	$ 960	$ (8,920)	$ 2,629	$ 34,629
Novartis collaboration deferred revenue	44,073	—	(46,985)	2,912	—
Ionis collaboration deferred revenue	3,587	—	—	253	3,840
Genentech collaboration deferred revenue	14,038	—	(14,681)	643	—
Total deferred revenue	$ 101,658	$ 960	$ (70,586)	$ 6,437	$ 38,469

	Beginning Balance January 1, 2024	Additions	Deductions	Impact of Exchange Rates	Ending Balance December 31, 2024
Contract liabilities:					
Deferred revenue					
Bayer collaboration deferred revenue	$ 43,618	$ 296	$ (3,393)	$ (561)	$ 39,960
Novartis collaboration deferred revenue	50,008	3,000	(8,161)	(774)	44,073
Ionis collaboration deferred revenue	12,464	90	(8,881)	(86)	3,587
Genentech collaboration deferred revenue	29,104	—	(14,840)	(226)	14,038
Total deferred revenue	$ 135,194	$ 3,386	$ (35,275)	$ (1,647)	$ 101,658

Contract assets represent research and development services which have been performed but have not yet been billed, and are reduced when they are subsequently billed. There were no contract assets at December 31, 2025 or 2024.

As of December 31, 2025, the Bayer and Ionis deferred revenue balances include $31.6 million and $3.8 million, respectively, allocated to material rights that will commence revenue recognition when the respective underlying options are exercised or when they expire.

During the years ended December 31, 2025, 2024 and 2023, the Company recognized revenues as a result of the following (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Revenue recognized in the period from:			
Revenue recognized based on proportional performance	$ 9,109	$ 24,266	$ 19,160
Revenue recognized based on contract modifications and expiration of material rights	61,477	10,576	7,816
Revenue recognized based on changes in transaction price	2,000	433	—
Total	$ 72,586	$ 35,275	$ 26,976

Cancer Research UK

BT1718

On December 13, 2016, the Company entered into a Clinical Trial and License Agreement with Cancer Research Technology Limited ("CRTL"), a wholly owned subsidiary of Cancer Research UK that Cancer Research UK's commercial activities operate through, and Cancer Research UK (the "BT1718 Cancer Research UK Agreement"). Pursuant to the BT1718 Cancer Research UK Agreement, as amended in March 2017 and June 2018, Cancer Research UK's Centre for Drug Development sponsored and funded a Phase I/IIa clinical trial for BT1718, a BDC molecule, in patients with advanced solid tumors. Upon the completion of the Phase I/IIa clinical trial, the Company had the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares. The Company was required to reimburse Cancer Research UK for certain costs upon specified termination events.

The Company concluded that the costs incurred by Cancer Research UK was a research and development funding liability in accordance with ASC 730, *Research and Development*, as certain payments were not based solely on the results of the research and development having future economic benefit.

On December 4, 2024, the Company, CRTL and Cancer Research UK entered into an Expiry and Revenue Sharing Agreement (the "BT1718 Expiration Agreement") pursuant to which (i) the Company did not exercise its option to obtain a license to the results of the clinical trial, (ii) CRTL did not elect to receive an assignment and exclusive license to develop and commercialize the product, and (iii) the BT1718 Cancer Research UK Agreement and all rights and obligations (other than certain surviving provisions as outlined in the agreement) under the BT1718 Cancer Research UK Agreement expired and terminated as of December 4, 2024. Under the terms of the BT1718 Expiration

Agreement, the Company agreed to pay to CRTL an upfront payment of $0.1 million. The Company will also pay to CRTL specified royalty and other payments at percentages in the very low to low single digits related to specified products targeting the MT1 target antigen.

The Company accounted for the BT1718 Expiration Agreement by applying the concepts of ASC 470, *Debt*. As all rights and obligations, including the Company's payment obligations, under the BT1718 Cancer Research UK Agreement expired and terminated, the Company concluded that the liability recorded under the BT1718 Cancer Research UK Agreement is extinguished as the Company has been legally released from being the primary obligor under the BT1718 Cancer Research UK Agreement. As such, the Company recognized a gain on extinguishment of the research and development funding liability of $4.5 million during the year ended December 31, 2024, which is recorded within other income, net, in the consolidated statements of operations and comprehensive loss.

10. Income taxes

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

	Year Ended December 31,		
	2025	2024	2023
United Kingdom	$ (225,456)	$ (179,610)	$ (182,980)
United States	6,648	5,814	3,773
Total	$ (218,808)	$ (173,796)	$ (179,207)

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

	Year Ended December 31,		
	2025	2024	2023
Current income tax provision (benefit)			
Federal - United States	$ 690	$ 283	$ (1,180)
State - United States	312	178	(669)
Total current income tax provision (benefit)	1,002	461	(1,849)
Deferred income tax (benefit) provision			
Federal - United States	(1,304)	(3,772)	2,513
State - United States	454	(1,454)	793
Total deferred income tax (benefit) provision	(850)	(5,226)	3,306
Total provision for (benefit from) income taxes	$ 152	$ (4,765)	$ 1,457

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

	Year Ended December 31, 2025	
	Amount ($)	Percent (%)
Provision for (benefit from) income taxes at U.K. federal statutory rate	$ (54,702)	25.0 %
Foreign tax effects		
United States	(1,513)	0.7 %
Changes in valuation allowances	19,869	(9.1)%
Nontaxable or nondeductible items		
Net losses surrendered for research credit	21,626	(9.9)%
Impact of foreign exchange rates	13,893	(6.3)%
Other	979	(0.5)%
Effective income tax rate	$ 152	(0.1)%

	Year Ended December 31,	
	2024	2023
(Benefit from) provision for income taxes at statutory rate	25.0 %	23.5 %
Increases (decreases) resulting from:		
Tax credits	3.7 %	0.6 %
Change in valuation allowance	(11.2)%	(14.8)%
Net losses surrendered for research credit	(14.2)%	(11.1)%
Impact of statutory rate change	— %	2.7 %
Impact of foreign exchange rates	(1.0)%	(0.1)%
Other	0.4 %	(1.6)%
Effective income tax rate	2.7 %	(0.8)%

Significant components of the Company's deferred tax assets are as follows (in thousands):

	December 31,	
	2025	2024
Deferred tax assets:		
Operating loss carryforwards	$ 101,324	$ 81,492
Research credit carryforwards	3,534	3,362
Operating lease liability	4,376	2,641
Share-based compensation	28,281	21,035
Depreciation & amortization	2,524	1,508
Accrued expenses and other	1,855	1,952
Total deferred tax assets	141,894	111,990
Deferred tax liabilities:		
Operating lease right-of-use asset	(4,165)	(2,201)
Total deferred tax liabilities	(4,165)	(2,201)
Valuation allowance	(126,761)	(99,672)
Net deferred tax assets	$ 10,968	$ 10,117

Cash paid for income taxes, net of refunds received, are as follows:

	Year Ended December 31,
	2025
Federal	$ —
State	—
Foreign	
United States	(717)
Total	$ (717)

During the years ended December 31, 2025, 2024 and 2023, the Company recorded an income tax provision of $0.2 million, an income tax benefit of $4.8 million and an income tax provision of $1.5 million, respectively. The Company is subject to U.K. corporate taxation. Due to the nature of its business, the Company has generated losses since inception and therefore not paid U.K. corporation tax. The provision for (benefit from) income taxes included in the consolidated statements of operations and comprehensive loss represents the tax impact from operating activities in the United States, which has generated taxable income based on intercompany service arrangements. Deferred tax assets benefitted in the United States do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement.

The Company's income tax provision recognized during the year ended December 31, 2025 is mainly the result of discrete items resulting from the workforce reduction in August 2025. The Company's income tax benefit recognized during the year ended December 31, 2024 is mainly the result of deferred tax assets 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, including incremental income tax benefits of approximately $3.5 million recognized during the year ended December 31, 2024 related to the completion of a U.S. research and development tax credit study. The Company's income tax provision recognized during the year ended December 31, 2023 is primarily related to the completion of an assessment, inclusive of an external tax analysis, during the year ended December 31, 2023, whereby the Company concluded that it is not required to capitalize certain research and development expenses incurred by its U.S. subsidiary associated with contractual research services performed on behalf of its U.K. subsidiary pursuant to an intercompany service arrangement because its U.S. subsidiary does not retain any ownership or rights in the underlying intellectual property resulting from the research services. The change in estimate upon the completion of this analysis resulted in the recognition of an income tax provision of $2.4 million during the year ended December 31, 2023.

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., the Company 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 its history of cumulative net profits in the United States and estimated future taxable income and has 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 by $27.1 million and $19.4 million in the years ended December 31, 2025 and 2024, respectively, due to the corresponding increases in U.K. deferred tax assets, primarily due to operating loss carryforwards generated during each 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, 2025 and 2024.

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 provision for (benefit from) 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 and U.K., U.S. 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, 2025, the Company had $405.3 million of U.K. operating loss carryforwards that have an indefinite life.

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 December 31, 2025 and 2024. 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 11 jurisdictions for state income taxes. In the normal course of business, the Company is subject to examination by tax authorities in these jurisdictions. The 2024 and 2023 tax years remain open to examination by the 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 2022 in the U.S. remain open to examination. The Company is currently not under examination by jurisdictions for any tax years.

11. Commitments and contingencies

Leases

In January 2023, the Company entered into a lease agreement for office and laboratory space in Cambridge, Massachusetts. The lease has a contractual period of approximately three years and the Company concluded that the lease term is three years, representing the non-cancelable lease period.

On December 6, 2021 the Company entered into a lease of new office and laboratory space, in Cambridge, United Kingdom. The lease has a contractual period of 10 years, but could be cancelled by the Company on the fifth anniversary of the lease commencement date. The Company concluded that the initial lease term was five years, representing the non-cancelable lease period. In December 2025, the Company entered into a deed of variation to the lease, pursuant to which (i) the Company elected not to cancel the lease on the fifth anniversary of the lease commencement date and (ii) the annual rent was increased effective in December 2026, payable quarterly in advance following a nine-month rent-free period from December 2026 to September 2027. The Company accounted for the deed of variation as a modification to the existing lease and remeasured the ROU asset and lease liability based on the present value of remaining lease payments, discounted at the Company's incremental borrowing rate on the modification date, and recognized an additional right-of-use asset and lease liability of $12.4 million during the year ended December 31, 2025. The Company has a contractual right to renew the lease for a further ten-year period, which also may be cancelled after five years.

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 was renewed in December 2021 for five years through December 2026. In April 2023, the Company entered into a deed of surrender related to the lease, pursuant to which the lease was terminated effective immediately. As a result of the deed, the Company derecognized the lease liability and right of use asset associated with the lease. The Company also paid termination-related fees of $0.3 million in connection with the deed, which were recorded as a loss on lease termination and are included in operating expenses in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2023.

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. In March 2022, Bicycle Therapeutics Inc. notified the landlord of its intent to exercise its option to extend the lease, originally set to expire on December 31, 2022, for a successive period through December 31, 2027. In May 2022, the lease was extended.

From time to time, the Company may enter into finance lease agreements for property and equipment. As of December 31, 2025 and 2024, the Company recorded finance lease right-of-use assets of $0.8 million and $1.0 million, respectively, which are included in property and equipment, net, in the consolidated balance sheets. As of December 31, 2025 and 2024, the Company recorded finance lease liabilities of $0.9 million and $1.0 million, respectively, which are included in accrued expenses and other current liabilities and other long-term liabilities, as applicable, in the consolidated balance sheets.

The components of the Company's lease expense are as follows (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Operating lease cost	$ 5,100	$ 5,299	$ 5,408
Variable lease cost	3,231	2,924	2,777
Finance lease cost:			
Amortization of finance lease right-of-use assets	217	53	—
Interest on finance lease liabilities	85	23	—
Total finance lease cost	$ 302	$ 76	$ —

The weighted average remaining operating lease term was 5.4 years and 2.0 years as of December 31, 2025 and 2024, respectively, and the weighted average operating lease discount rate was 6.4% and 7.8% as of December 31, 2025 and 2024, respectively. The weighted average remaining finance lease term was 3.7 years and 4.7 years as of December 31, 2025 and 2024, respectively, and the weighted average finance lease discount rate was 9.5% and 9.5% as of December 31, 2025 and 2024, respectively.

The following table summarizes the maturities of the Company's lease liabilities as of December 31, 2025 (in thousands):

Year Ending December 31,	Operating Leases	Finance Leases
2026	3,463	274
2027	2,874	274
2028	3,654	274
2029	3,654	206
2030	3,654	—
2031	2,515	—
Present value adjustment	(3,167)	(154)
Total lease liabilities	16,647	874
Less: current lease liabilities	(2,551)	(205)
Long term lease liabilities	$ 14,096	$ 669

Other commitments

The Company has entered into various agreements with contract research organizations to provide clinical trial services, contract manufacturing organizations to provide clinical trial materials and with vendors for preclinical research studies, synthetic chemistry and other services for operating purposes. These 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. In some cases, the Company is contractually obligated to make certain minimum payments to the vendors, based on the timing of the termination notification and the exact terms of the agreement.

The Company has also entered into separate agreements with third parties which provide for various future milestone payments upon the achievement of specified development, regulatory, commercial and sales-based milestones with an aggregate total value of $105.8 million, as well as potential future royalty and other payments at percentages ranging from very low to low single digits. These additional milestone payments are contingent upon future events that are not considered probable of achievement as of December 31, 2025. As of December 31, 2025, the Company was unable to estimate the timing or likelihood of achieving these milestones.

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. The Company is not currently

subject to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of ASC 450, *Contingencies*.

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 and officers 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. In addition, the Company has agreed to indemnify certain investors in limited circumstances. 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, 2025 and 2024.

12. Net loss per share

Basic and diluted net loss per share was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,		
	2025	2024	2023
Numerator:			
Net loss	$ (218,960)	$ (169,031)	$ (180,664)
Denominator:			
Weighted average ordinary shares outstanding, basic and diluted	69,279,838	58,207,593	35,592,362
Net loss per share, basic and diluted	$ (3.16)	$ (2.90)	$ (5.08)

The Company's potentially dilutive securities, which include options to purchase ordinary shares and restricted share units for ordinary 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, which includes both ordinary shares and non-voting ordinary shares, used to calculate both basic and diluted net loss per share 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 for the periods indicated because including them would have had an anti-dilutive effect:

	December 31,		
	2025	2024	2023
Restricted ordinary shares	1,644,421	716,262	326,848
Options to purchase ordinary shares	9,803,106	8,748,726	7,469,527
	11,447,527	9,464,988	7,796,375

13. 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, 2025, 2024 and 2023, the Company made contributions totaling $1.2 million, $1.1 million and $0.8 million, respectively, to the 401(k) Plan.

The Company provides a pension contribution plan for its employees in the United Kingdom, pursuant to which the Company may make contributions each year ("U.K Plan"). During the years ended December 31, 2025, 2024 and 2023, the Company made contributions totaling $3.9 million, $2.9 million and $2.2 million, respectively, to the U.K. Plan.

14. Related party transactions

Amendment to Consulting Agreement with Stone Atlanta Estates LLC

Pierre Legault, former Chairman of the Company's board of directors, is associated with Stone Atlanta Estates LLC, which provided consultancy services to the Company totaling $0.1 million during the year ended December 31, 2025 prior to Mr. Legault's retirement as Chairman of the Company's board of directors. Stone Atlanta Estates LLC provided consultancy services to the Company totaling $0.3 million and $0.2 million during the years ended December 31, 2024 and 2023, respectively. In March 2025, the Company and Mr. Legault entered into an amendment to the consulting agreement, effective as of June 17, 2025, the date of Mr. Legault's retirement as Chairman. The amendment modified the compensation payable under the agreement and provides for expiration of the agreement to be no later than June 30, 2028.

Related Party Participation in Private Placement

The Investors in the Private Placement included certain entities affiliated with Baker Bros. Advisors LP (the "Baker Entities"), an entity which may be deemed a beneficial owner of greater than 10% of the Company's voting securities. Felix J. Baker, the current Chairman of the Company's board of directors, is a managing member of Baker Bros. Advisors (GP) LLC, the sole general partner of Baker Bros. Advisors LP. In the Private Placement, the Baker Entities purchased an aggregate of 17,114,846 non-voting ordinary shares, nominal value £0.01 per share, for an aggregate purchase price of $366.6 million. The Private Placement was approved in accordance with the Company's related person transaction policy by the Company's Related Parties Committee. See Note 11. "Commitments and contingencies" for additional information on indemnities provided to certain investors.

15. Segments and geographic information

The Company operates and manages its business as a single operating segment, which is developing a unique class of chemically synthesized medicines based on its proprietary platform. The Company's chief operating decision maker ("CODM") is the Company's Chief Executive Officer ("CEO"). The CODM reviews consolidated operating results, manages the business on a consolidated basis and utilizes consolidated net loss from the consolidated statements of operations and comprehensive loss as the primary measure of segment profit or loss in making decisions surrounding allocating resources and assessing performance of the Company. The CODM is regularly provided detailed expense information, including expenses by program and expense category, and the CODM makes decisions surrounding capital and personnel allocation using this information on a consolidated basis.

The following table presents information about the Company's single operating segment, including significant segment expenses, for the years ended December 31, 2025, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Collaboration revenue	$ 72,586	$ 35,275	$ 26,976
Significant segment expenses:			
Research and development:			
Zelenectide pevedotin (Nectin-4)	126,780	82,705	44,135
Nuzefatide pevedotin (EphA2)	8,487	9,119	9,195
Bicycle tumor-targeted immune cell agonists	1,991	7,840	18,878
Discovery, platform and other expense	43,221	30,293	37,815
Employee and contractor related expenses	69,701	58,687	46,506
Share-based compensation	18,024	19,424	15,581
Facility expenses	6,999	8,105	8,845
Research and development incentives and government grants	(34,920)	(43,207)	(24,459)
Total research and development	240,283	172,966	156,496
General and administrative:			
Personnel-related costs	28,358	23,500	18,985
Professional and consulting fees	20,646	20,258	14,814
Other general and administrative costs	9,577	9,047	9,137
Share-based compensation	21,440	18,657	16,896
Effect of foreign exchange rates	(653)	719	594
Total general and administrative	79,368	72,181	60,426
Total significant segment expenses	319,651	245,147	216,922
Other segment items[(1)]	28,105	40,841	9,282
Net loss	$ (218,960)	$ (169,031)	$ (180,664)

(1) Other segment items include interest and other income, interest expense, loss on extinguishment of debt, gain on extinguishment of research and development funding liability and provision for (benefit from) income taxes.

The Company does not regularly provide the CODM with detailed segment asset information other than what is included in the consolidated balance sheets. Please refer to the consolidated financial statements and the accompanying notes to the consolidated financial statements for segment asset information.

The Company operates in two geographic regions: the United States and the United Kingdom. Information about the Company's long-lived assets, including operating lease ROU assets, held in different geographic regions is presented in the table below (in thousands):

	December 31,	
	2025	2024
United States	$ 863	$ 3,037
United Kingdom	21,044	14,152
	$ 21,907	$ 17,189

The Company's collaboration revenue is attributed to the operations of the Company in the United Kingdom.

16. Subsequent events

In March 2026, the Company announced the strategic reprioritization of its clinical portfolio to focus on its promising pipeline of next-generation therapeutics, including nuzefatide pevedotin as well as next-generation Bicycle conjugates, including BRC molecules. In conjunction with its strategic reprioritization, the Company is implementing a proposed workforce reduction of approximately 30% of its workforce. Together, the workforce reduction and strategic reprioritization are expected to reduce the Company's annual operating expenses by approximately 50% based on the

Company’s current plans. The Company expects the workforce reduction to be substantially completed by the end of 2026 and to recognize aggregate charges for severance and other employee termination benefits of approximately $8.0 million.

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 17, 2026

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

/s/ Travis Thompson
Travis Thompson
Chief Financial Officer (Principal Financial and Accounting Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Kevin Lee and Travis Thompson, 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 17, 2026
/s/ Travis Thompson Travis Thompson	Chief Financial Officer (Principal Financial and Accounting Officer)	March 17, 2026
/s/ Felix J. Baker Felix J. Baker, Ph.D	Chairman of the Board and Director	March 17, 2026
/s/ Janice Bourque Janice Bourque, MBA	Director	March 17, 2026
/s/ Roger Dansey Roger Dansey, M.D.	Director	March 17, 2026
/s/ Jose-Carlos Gutierrez-Ramos Jose-Carlos Gutierrez-Ramos, Ph.D	Director	March 17, 2026
/s/ Hervé Hoppenot Hervé Hoppenot	Director	March 17, 2026
/s/ Alessandro Riva Alessandro Riva, M.D.	Director	March 17, 2026
/s/ Stephen Sands Stephen Sands, MBA	Director	March 17, 2026
/s/ Charles Swanton Charles Swanton, M.D., Ph.D., FRS, FMedSci, FRCP	Director	March 17, 2026
/s/ Sir Gregory Winter Sir Gregory Winter, FRS	Director	March 17, 2026

EXECUTIVE TEAM

Kevin Lee, PhD, MBA
Chief Executive Officer

Travis Thompson
Chief Financial Officer

Michael Hannay, DSc
Chief Product and Supply Chain Officer

Jennifer Perry, PharmD
Chief Operating Officer

Michael Skynner, PhD
Chief Scientific Officer

BOARD OF DIRECTORS

Felix J. Baker, PhD
Managing Member, Baker Bros. Advisors LP

Janice Bourque, MBA
Former Managing Director, Hercules Capital

Roger Dansey, MD
Director, Nurix Therapeutics, Inovio Pharmaceuticals

Jose-Carlos Gutierrez Ramos, PhD
Chief Scientific Officer, Danaher

Hervé Hoppenot
Chairman, Maze Therapeutics

Kevin Lee, PhD, MBA
Chief Executive Officer, Bicycle Therapeutics

Alessandro Riva, MD
Chief Executive Officer & Chairman, Transgene S.A.

Stephen Sands, MBA
Managing Director, Skia Capital

Charles Swanton, MD, PhD, FRS, FMedSci, FRCP
Deputy Clinical Director & Principal Group Leader, The Francis Crick Institute

Sir Gregory Winter, FRS
Co-Founder, Bicycle Therapeutics

INVESTOR RELATIONS
Matthew DeYoung, Argot Partners
ir@bicycletx.com

FORM 10K
A copy of our Form 10-K filed with the SEC on March 17, 2026 will be made available to all shareholders at no charge.

The Form 10-K also can be accessed through the SEC website at www.sec.gov, or through the Investor section of our website at investors.bicycletherapeutics.com.

To receive a copy by mail please contact Investor Relations at ir@bicycletx.com.

WEBSITE
www.bicycletherapeutics.com

CHIEF LEGAL OFFICER AND GENERAL COUNSEL
Zafar Qadir

INDEPENDENT PUBLIC ACCOUNTING FIRM
PricewaterhouseCoopers LLP

ANNUAL GENERAL MEETING
Our annual meeting of shareholders will be held on Wednesday, June 17, 2026, at 2:00 p.m. London time (9:00 a.m. Eastern Daylight Time), at our principal executive offices, located at Blocks A & B, Portway Building, Granta Park, Great Abington, Cambridge, CB21 6GS, United Kingdom.

STOCK INFORMATION
Nasdaq Global Select Market: BCYC

ADDRESS
Blocks A & B Portway Building, Granta Park, Great Abington, Cambridge, CB21 6GS, United Kingdom