

Risk Factors Comparison 2025-02-25 to 2024-02-20 Form: 10-K

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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.
- ~~Our failure to comply with the covenants or payment obligations under our existing term loan facility with Hercules Capital, Inc., or Hercules, could result in an event of default, which may result in increased interest charges, acceleration of our repayment obligations or other actions by Hercules, any of which could negatively impact our business, financial condition and results of operations.~~
- We are substantially dependent on the success of our internal development programs and of our product candidates from our Bicycle® Toxin Conjugate, or BTC®, and Bicycle Tumor- Targeted Immune Cell Agonist®, or Bicycle TICA®, 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.
- **47** • 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.
- ~~47~~ • 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 clinical research organizations, or 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, 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. ● 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 based outside of the United States, we are subject to economic, political, regulatory and other risks associated with international operations. **Risks** ~~48~~**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 \$ **169.0 million**, \$ 180.7 million, ~~and~~ \$ 112.7 million ~~and~~ \$ 66.8 million for the years ended December 31, **2024**, 2023, ~~and~~ 2022 ~~and~~ 2021, respectively. As of December 31, ~~2023~~ **2024**, ~~we the Company~~ had an accumulated deficit of \$ ~~511.680~~ .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 BTC and Bicycle TICA programs and our other pipeline programs, **including for the ongoing Phase II / III Duravelo- 2 registrational trial**; ● initiate and continue research, preclinical and clinical development efforts for any future product candidates; ~~48~~ ● 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~~ ~~49~~**and** any collaborators may never succeed in these activities and, even if we do, or any collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our revenue to date has been primarily generated from our research collaborations with Bayer Consumer Care AG, or Bayer, Novartis Pharma AG, or Novartis, Ionis Pharmaceuticals, Inc., or Ionis, **and** Genentech Inc., or Genentech, ~~Dementia Discovery Fund, or DDF, Sanofi (formerly Bioverativ Inc.), AstraZeneca AB, or AstraZeneca, and Oxurion NV, or Oxurion~~. 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 ~~49~~**companies** ~~companies~~ in the early stages of development, especially clinical- stage ~~biopharmaceutical~~ ~~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~~ **50any** 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 \$ ~~526-879~~ **4-5** million as of December 31, ~~2023-2024~~, 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; ~~50~~ • the number of future product candidates that we pursue and their development requirements; • the outcome, timing and costs of seeking regulatory approvals; • the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities; • subject to receipt of marketing approval, revenue, if any, received from commercial sales of our current and future product candidates; • our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure; • the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights including enforcing and defending intellectual property related claims; and • the costs of operating as a public company. While the long- term economic impact of public health crises or geographical tensions and wars, such as the ~~Russia-ongoing wars involving~~ **Ukraine war and the Israel-Hamas war**, 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, have increased recently to levels not seen in decades. Increased inflation may result in increased operating costs (including labor costs) and may affect our operating budgets. In addition, the U. S. Federal Reserve has raised, and may further raise, interest rates in response to concerns about inflation. 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. ~~On March 10, 2023, in addition to the failure of SVB-UK, its parent company, Silicon Valley Bank, also failed, and Signature Bank failed on March 12, 2023. Although the U. K. and U. S. governments both took steps to guarantee all depositors at these banks, there is no guarantee that these governments or any other government would guarantee depositors in the event of further bank closures, and continued instability in the global banking system may adversely impact our business and financial condition. If the disruptions, instability and slowdown deepen or persist, we may not be able to access our cash as needed or to raise additional capital on favorable terms, or at all, which could in the future negatively affect our financial condition and our ability to pursue our business strategy.~~ 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~~ **51additional** 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 ~~51~~ **development** or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. ~~Our failure to comply with the covenants or payment obligations under our existing term loan facility with Hercules could result in an event of default, which may result in increased interest charges, acceleration of our repayment obligations or other actions by Hercules, any of which could negatively impact our business, financial condition and results of operations. We are party to a secured term loan facility with Hercules. As of December 31, 2023, our outstanding borrowings under this facility totaled \$ 30. 0 million. In connection with the Loan and Security Agreement, as amended, with Hercules, or the Loan Agreement, we granted Hercules a security interest in substantially all of our personal property and other assets, other than our intellectual property. The Loan Agreement contains customary affirmative and restrictive covenants and representations and warranties, including a covenant against the occurrence of a change in control (as defined by the Loan Agreement), financial reporting obligations, and certain limitations on indebtedness, liens (including a negative pledge on intellectual property and other assets), investments, distributions (including dividends), collateral, investments, transfers, mergers or acquisitions, taxes, corporate changes, and deposit accounts. The Loan Agreement also includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, the occurrence of certain events that could reasonably be expected to have a material adverse effect as set forth in the Loan Agreement, cross acceleration to third-party indebtedness and certain events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, a default interest rate of an additional 5. 0 % may be applied to the outstanding principal and interest payments due, and Hercules may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement, including proceeding against the collateral securing such indebtedness. Such increased interest charges, accelerated repayment, proceedings against the collateral or other actions may have a negative impact on our business, financial condition and results of operations. Our existing and any future indebtedness may limit our cash flow available to invest in the ongoing needs of our business. As of December 31, 2023, we had \$ 30. 0 million of borrowings outstanding under the Loan Agreement with an interest rate that is capped at 9. 05 %. We could also in the future incur additional indebtedness pursuant to additional loan agreements. Our debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including: • requiring us to dedicate cash flow from operations or cash on hand to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes; • increasing our vulnerability to adverse changes in general economic, industry and market conditions; • subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing; • limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and • placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options. We intend to satisfy our current and future debt service obligations with our existing cash and funds from external sources. Nonetheless, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing or any future debt facility. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under the Loan Agreement or any future ~~52~~ loan agreements we may enter into could result in an event of default and acceleration of amounts due. If an event of default occurs and the lenders accelerate the amounts due under such loan agreements, we may not be able to make accelerated payments, and such lenders could seek to enforce security interests in the collateral securing such indebtedness.~~ Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates We are substantially dependent on the success of our internal development programs and of our product candidates from our BTC and Bicycle TICA programs, which may not successfully complete clinical trials, receive regulatory approval or be successfully commercialized. Our future success will depend heavily on the success of our internal development programs and of product candidates from our BTC and Bicycle TICA programs. Within our BTC programs, we are evaluating **zelenectide pervedotin, formerly** BT8009, a BTC molecule that targets Nectin- 4 and carries a monomethyl auristatin E, or 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 Nectin- 4 expressing advanced malignancies and **a an ongoing** Phase II / III registrational trial called Duravelo- 2 ~~which is now active and recruiting patients~~, and BT5528, a BTC 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 associated with EphA2 expression. ~~In addition, BT1718, a BTC molecule designed to target tumors that express MT1- MMP, is being investigated for safety, tolerability and efficacy in a Phase I / IIa clinical trial sponsored and fully funded by the Cancer Research UK Centre for Drug Development, or Cancer Research UK. Upon the completion of the Phase I / IIa clinical trial for BT1718, we have the right to obtain a license to the results of the clinical trial from Cancer Research UK upon the payment of a milestone, in cash and ordinary shares with a combined value in a mid- six digit dollar amount. If we do not exercise our right to obtain a license to the results of the clinical trial or we fail to obtain a license, our ability to continue development of BT1718 would be negatively impacted.~~ We are also evaluating BT7480, ~~which is~~ a Bicycle TICA molecule targeting Nectin- 4 and agonizing CD137, 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. There can be no assurance our BTC molecules or Bicycle TICA 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 European Medicines Agency, or EMA, in Europe or similar regulatory authorities will approve our BTC 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 BTC molecules, Bicycle TICA molecules, and our other product candidates, **including our BRC molecules**, 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 EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each EU Member State, leading to a single decision for each EU Member State. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment by all EU Member States concerned, and a separate assessment by each EU Member State with respect to specific requirements related to its own territory, including ethics rules. Each EU Member State's decision is communicated to the sponsor via the centralized EU portal. Once the clinical trial is approved, clinical study development may proceed. The CTR foresees a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials in relation to which application for approval was made on the basis of the Clinical Trials Directive before January 31, 2023, the Clinical Trials Directive ~~will continue~~ **continued** to apply on a transitional basis until January 31, 2025. ~~By that, by which~~ **date**, all ongoing trials ~~will be~~ **under the Clinical Trials Directive** ~~become~~ **became** subject to the provisions of the CTR ~~and all new~~. ~~The CTR will apply to clinical trials since from an earlier date if the related clinical trial application was made on the basis of the CTR or if the clinical trial has already transitioned to the CTR framework before January 31, 2025~~ **2023 have been subject to the CTR**. Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. ~~In light of the entry into application of the CTR on January 31, 2022, we may be required to transition clinical trials for which we have obtained regulatory approvals in accordance with the CTD to the regulatory framework of the CTR. Transition of clinical trials governed by the CTD to the CTR will be required for clinical trials which will have at least one site active in the EU on January 30, 2025. A transitioning application would need to be submitted to the competent authorities of EU Member States through the Clinical Trials Information Systems and related regulatory approval obtained to continue the clinical trial past January 30, 2025. This requires financial, technical and human resources. If we are unable to transition our clinical trials in time, the conduct of those clinical trials may be negatively impacted. In addition, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing 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 recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a ~~54decrease~~ **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 .

53The U. K.'s regulatory framework in relation to clinical trials is derived from existing legislation of the EU (as implemented into the law of the U. K., through secondary legislation). On January 17, 2022, the MHRA launched an eight- week consultation on reframing the U. K.'s legislation for clinical trials. The U. K.'s government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These changes were laid before parliament on December 12, 2024 and if adopted will bring the U. K. into closer alignment with the EU. 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 European Economic Area**, or EEA, ~~countries, in the EEA,~~ 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~~ **54sites** 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. ~~55~~ ~~We~~ **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 ~~55~~ 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 ~~56~~ ~~indications~~ **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 ~~BT8009~~ **zelenetide pevedotin**, BT5528, ~~and~~ BT7480 ~~and~~ BT1718 is currently taking place outside of the United States. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including: ~~56~~ • difficulty in establishing or managing relationships with academic partners or contract research organizations, or CROs, and physicians; • different standards for the conduct of clinical trials; • the absence in some countries of established groups with sufficient regulatory expertise for review of protocols related to our novel approach; ~~57~~ • 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, our company-sponsored Phase I / II clinical trials of ~~BT8009~~ **zelenetide pevedotin**, BT5528 and BT7480 are ongoing ~~and~~ BT1718 is being investigated in a Phase I / IIa trial conducted by ~~Cancer Research UK~~, and the interim results of these trials, 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. While we ~~have~~ aligned with the FDA on the design of a Phase II / III registrational trial for ~~BT8009~~ **zelenetide pevedotin**, called Duravelo-2, which is ~~currently enrolling~~ **now active and recruiting patients**, we otherwise have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. Preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, 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. We do not develop companion diagnostics internally and thus we will be dependent on the sustained ~~cooperation~~ **57** **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 ~~58~~~~both~~ **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. ~~Four~~ **Three** of our product candidates are currently undergoing safety testing in the form of ~~Phase I / II~~ **Phase I / II**, 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 ~~BT8009~~ **zelenectide pevedotin**, BT5528, BT7480, ~~BT1718~~ or any other of our product candidates are safe in humans. Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less ~~effective~~ **58effective** 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; ~~59~~ ● 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 August 2024, we focused our research and development pipeline on clinical programs and research areas that we believe have the highest potential to maximize value creation and we consolidated all discovery research activities to our headquarters in Cambridge, U. K. Moving forward, we will prioritize the clinical development of BTC molecules in multiple tumor types and focus our near-term research efforts on advancing our BRC pipeline and the discovery of next-generation BTC molecules**. 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** ~~potential~~ **59potential** 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 **recent** 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. ~~60~~ **We** ~~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~~ **60product** 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 ~~61~~ ~~unmet~~ **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~~ **61 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 ~~62 or~~ **62 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. The withdrawal of the ~~United Kingdom~~ **U. K.** from the EU, commonly referred to as “Brexit,” may adversely impact our ability to obtain regulatory approvals of our product candidates in the EU, result in restrictions or imposition of taxes and duties for importing our product candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU. Following Brexit, the ~~UK~~ **U. K.** and the EU signed a EU- ~~UK~~ **U. K.** Trade and Cooperation Agreement, or TCA, which became provisionally applicable on January 1, 2021, and entered into force on May 1, 2021. The TCA primarily focuses on ensuring free trade between the EU and the ~~UK~~ **U. K.** in relation to goods, including medicinal products. Among the changes that have occurred are that ~~the U. K. Great Britain (England, Scotland and Wales)~~ **the U. K.** is treated as a “third country,” a country that is not a member of the EU and whose citizens do not enjoy the EU right to free movement. Northern Ireland continues to follow ~~certain limited~~ **certain limited** many aspects of the EU regulatory rules, ~~particularly including~~ **particularly including** in relation to ~~trade~~ **trade** ~~medical devices, but not~~ **medical devices, but not** ~~in goods~~ **relation to** ~~medicinal products~~ **medicinal products**. As part of the TCA, the EU and the ~~UK~~ **U. K.** recognize GMP inspections carried out by the other party and the acceptance of official GMP documents issued by the other party. The TCA also encourages, although it does not oblige, the parties to consult one another on proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The ~~UK~~ **U. K.** has unilaterally agreed to accept EU batch testing and batch release. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the ~~UK~~ **U. K.** must be retested and re-released when entering the EU market for commercial use. ~~As it relates to marketing authorizations, Great Britain has a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland continues, however, to be covered by the marketing authorizations granted by the European Commission. For example, the scope of a marketing authorization for a medicinal product granted by the European Commission or by the competent authorities of EU Member States no longer encompasses Great Britain (England, Scotland and Wales). In these circumstances, a~~

separate marketing authorization granted by the UK competent authorities is required to place medicinal products on the market in Great Britain. Northern Ireland continues, however, to be covered by the marketing authorizations granted by the European Commission. On February 27, 2023, the UK U. K. government and the European Commission reached a political agreement on the so-called "Windsor Framework." The Windsor framework Framework is intended to revise the Northern Ireland Protocol to address some of the perceived shortcomings in its operation. The agreement was adopted at the Withdrawal Agreement Joint Committee on March 24, 2023. ~~If the changes are adopted in the form proposed, and the arrangements under the Windsor Framework relating to medicinal products took effect to be placed on the January 1, 2025. As it relates to market marketing in authorizations,~~ the UK will be authorized solely in accordance with UK laws U. K. has a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland continued, until January 1, 2025, would be reintegrated back into a UK-only regulatory environment under the authority of the MHRA with respect to all medicinal products. The implementation of ~~be covered by the marketing authorizations granted by the European Commission but~~ the Windsor Framework would occur in stages, with new arrangements 62 provides that the MHRA is the sole regulatory body responsible for relating -- granting marketing authorizations for to the supply of medicinal products into Northern Ireland anticipated to take effect in as of January 1, 2025. 63A A significant proportion of the regulatory framework in the UK U. K. applicable to medicinal products is currently derived from EU Directives and Regulations. The potential for UK U. K. legislation to diverge from EU legislation following Brexit could materially impact the regulatory regime with respect to the development, manufacture, import, approval, and commercialization of our product candidates in the UK U. K. or the EU. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. All of these changes could increase our costs and otherwise adversely affect our business. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the UK U. K. or the EU and restrict our ability to generate revenue and achieve and sustain profitability. In addition, we may be required to pay taxes or duties or be subjected to other hurdles in connection with the importation of our product candidates into the EU. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK U. K. or the EU for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import / export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK U. K. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU. 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 63FDA 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 64administrative -- 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; 64 • 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 65 -- 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 BT8009 zelnecotide pevvedotin, BT5528, BT7480, BT1718 and any other product candidates we develop as a therapy for patients who have received one or more prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first- line therapy, but there is no guarantee that product candidates we develop, even if approved, would be approved for first- line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials. The number of patients who have the cancers we are targeting may turn out to be lower than expected. Additionally, the potentially addressable patient population for our current programs or future product candidates may be limited, if and when approved. Even if we obtain significant market share for any product candidate, if and when approved, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications, including use as first- or second- line therapy. Even if we receive marketing approval of a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products, if approved. Any marketing approvals that we receive for any current or future product candidate may be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval, or contain requirements for potentially costly post- market testing and surveillance to monitor the safety and efficacy of the product candidate. The FDA 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 laws⁶⁵ 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 physicians⁶⁶ 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 pharmaceutical⁶⁶ 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. ~~67~~ 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 multinational companies as well as large biotechnology companies are developing programs for the targets that we are exploring for our BTC 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, Corbus Pharmaceutical Holdings, Inc., Innate Pharma SA and Mabwell Therapeutics, Inc. Furthermore, many companies are developing programs for CD137 or CD137 bi-specific antibodies or antibody fragments. 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 biopharmaceutical⁶⁷ 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; ~~67~~ • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; ~~68~~ • the strength of marketing and distribution support and timing of market introduction of competitive products; • publicity concerning our products or competing products and treatments; and • sufficient third-party insurance coverage and adequate reimbursement. Even if a product candidate displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product, if approved for commercial sale, will not be known until after it is launched. Our efforts to educate the medical community and payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors, particularly due to the novelty of our Bicycle approach. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer. We currently focus our research and product development on treatments for oncology indications and our product candidates are designed to target specific tumor antigens. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, ~~are~~ ~~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~~ ~~68~~ ~~There~~ is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, as the CMS decides whether and to what extent a new ~~69~~ ~~medicine~~ ~~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 drug practices. Specifically, there have been several recent U. S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. **Our results of operations could be adversely affected by the Patent Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, the Inflation Reduction Act of 2022, or the IRA, and by other healthcare legislative reforms that may be enacted or adopted in the future, particularly in light of the recent U. S. Presidential and Congressional elections.** 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. **In December 2021, Regulation No 2021 / 2282 on HTA amending Directive 2011 / 24 / EU, was adopted in the European Union. This Regulation, which entered into force in January 2022 and applies as of January 12, 2025, is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the level of the European Union for joint clinical assessments in these areas. The Regulation permits Member States to use common HTA tools, methodologies, and procedures across the European Union, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. 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. 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, Regulation No 2021 / 2282 on HTA does not apply in the U. K. However, the U. K. Medicines and Healthcare products Regulation Agency, or 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, including, effective as of March 31, 2025, relaunching the Innovative Licensing and Access Pathway with more predictable timelines and closer involvement of the National Health Service.** 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~~ **70** 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 **1** 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 ~~71~~ **may** be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to: • the Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. “ Remuneration ” has been interpreted broadly to include anything of value. A person or entity does not need to have actual knowledge of the Anti- Kickback Statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA, or federal civil money penalties. The Anti- Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution; • the 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; **71** • 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; 72 • 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, 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 the data privacy and security laws ~~we~~ **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, ~~some of whom receive share options as compensation for services provided,~~ are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, imprisonment, exclusion from participation in federal and state healthcare programs (such as Medicare and Medicaid), additional reporting requirements and / or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws, and 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. ~~73Healthcare~~ **Healthcare** legislative reform measures may have a negative impact on our business and results of operations. In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post- approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products, (iv) restriction on coverage, reimbursement, and pricing for our products, (v) transparency reporting obligations regarding transfers of value to health care professionals or (vi) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect our business, financial condition and results of operations. Among policy makers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and / or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. **In March For example, the ACA, which was signed into law in 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers a sweeping law intended to broaden access to health insurance**, and significantly impacts **reduce or constrain** the U. S. pharmaceutical **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. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, created a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid-managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand- **and impose additional health policy reforms** drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. There have been executive, judicial and Congressional challenges **and amendments** to certain aspects of ACA. For example, on June 17, 2021, the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the U. S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or the IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket costs and creating a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the **Biden-new Trump** administration will impact the ACA and our business. **In 73** In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA and the Consolidated Appropriations Act of 2023, will remain in effect through 2032 unless additional Congressional action is taken. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 **was signed** into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, **beginning effective** January 1, 2024. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. **74** There **There** has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. **The** Specifically, there have been several recent U. S. Congressional inquiries, Presidential executive orders and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer-patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U. S. Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (i) allows HHS to negotiate the price of certain high-expenditure drugs and biologics **that have been on the market for at least seven years and** covered under Medicare, and subjects drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law, and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions **began to** take effect progressively starting in 2023. On August **29-15, 2023-2024**, HHS announced the **list agreed-upon prices** of the first **ten-10** drugs that **were will be** subject to price negotiations, **although which take effect in January 2026. HHS will select up to 15 additional products covered under Part D for negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to** the Medicare drug price negotiation program is currently subject to legal challenges. It is currently unclear how the IRA will be effectuated but it is likely to have a significant impact on the pharmaceutical industry. Further, in response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. Similarly, individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient

~~reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures~~. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation, administrative or executive action. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates. We are subject to the U. K. Bribery Act 2010, or the Bribery Act, the U. S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, and other anti- corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations. Our operations are subject to anti- corruption laws, including the Bribery Act, the FCPA, the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, and other anti- corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us, our employees and our intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited ~~payments~~ **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~~ **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 or 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~~ **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)~~ **(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. 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. ~~In the past few years, numerous~~ **Numerous** U. S. states — ~~including California, Virginia, Colorado, Connecticut, and Utah~~ — 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”)~~ **(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 ~~(of up to \$ 7, 500 per intentional violation)~~ **and** ~~and~~ allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data

processed in the context of clinical trials, the CCPA increases compliance costs and potential liability with respect to other personal data maintained by covered entities about California residents. 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, and these developments may further complicate compliance efforts and may increase legal risk and compliance costs for us and the third parties ~~upon with whom we rely work~~. ~~Outside 75~~~~Outside~~ of the ~~United States~~ ~~U. S.~~, 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 ~~UK~~ ~~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 are considering and may adopt similar laws. Our employees and personnel may 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 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.~~ ~~United Kingdom~~, or the ~~UK~~, 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 ~~UK~~ ~~U. K.~~ to the United States in compliance with law, such as the European Commission's Standard Contractual Clauses, the ~~UK~~ ~~U. K.~~ International Data Transfer Agreement and the ~~UK~~ ~~U. K.~~ Transfer Addendum, the EU- U. S. Data Privacy Framework and the ~~UK~~ ~~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, ~~UK~~ ~~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 ~~UK~~ ~~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. 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** ~~regarding~~ data privacy and security. **If 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 76~~**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 that process personal data on our behalf**. 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 ~~on with whom we rely work~~ may fail to comply with such ~~77~~~~Obligations~~ **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. **For example, any failure by a third-party processor to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including inability to or interruption in our ability to operate our business and proceedings against us by governmental entities or others.** If we or the third parties ~~on which~~ **with whom** we ~~rely 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 U. S.**, 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~~ **77Although** 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 ~~78result~~ **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 ~~United Kingdom~~ **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 ~~UK~~ **U. K.** GDPR governing the use, processing, and cross- border transfer of personal data; ● changes in non- U. S. regulations and customs, tariffs and trade barriers; ● changes in non- U. S. currency exchange rates of the pound sterling, U. S. dollar, euro and currency controls; ● changes in a specific country’ s or region’ s political or economic environment, including the implications of Brexit **and the recent presidential election in the United States**; ● 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; **78** ● 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; ~~79~~ ● 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 ~~increased after~~ **increased after continues as a result of the** Russia ~~invaded~~ **invaded** Ukraine **and in February 2022. In** response to the **Hamas- Israel wars** invasion, North Atlantic Treaty Organization, or NATO, has ~~as~~ **as** deployed additional military forces to Eastern Europe **well as the conflicts in the Middle East**, including **between Israel** to Lithuania, and

Hezbollah the United Kingdom, the European Union and the United States implemented certain sanctions against Russia. The **These wars** invasion of Ukraine and the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries have created global security concerns that could result in a regional conflict and otherwise 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** the conflict has had significant ramifications on global financial markets, which may adversely impact our ability to raise capital in the future on favorable terms or at all. Cyber- attacks, **failures in or interruptions of**, or other **compromise to** failures in telecommunications or our information technology systems and deficiency in our, or those of third parties upon which with whom we rely work, cybersecurity 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 upon which with whom we rely work and may process proprietary, confidential, and sensitive data, including personal data (such as health- related data), intellectual property, and trade secrets (collectively, 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 upon which with whom we rely 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 upon which with whom we rely 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 upon which with whom we rely 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, 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 become more common and 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 ⁷⁹affected 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. ⁸⁰In 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 may 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 may 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 upon which with whom we rely 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 upon which we rely. **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 upon which we rely) 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 ~~are~~ **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 upon which we rely) 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~~ **our 80our** 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 81** ~~In addition to experiencing a security incident,~~ **third parties may gather, collect, or our infer** sensitive information **about us from public sources, including personal** data brokers, ~~or other means that reveals competitively sensitive details about our organization and 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 to undermine our competitive advantage or market position.~~ 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, artificial intelligence, or AI, based platforms are increasingly being used in the ~~biopharmaceutical~~ **pharmaceutical** industry. While we have introduced measures to restrict the internal use of public AI platforms, they may be used by our vendors, suppliers and contractors with access to our proprietary and confidential information, including trade secrets. Such use 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. Exchange rate fluctuations may materially affect our results of operations and financial condition. Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U. S. dollar, may adversely affect us. Although we are based in the ~~United Kingdom~~ **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 will depend, on development and commercialization collaborators to develop and conduct clinical trials with, obtain regulatory approvals for, and if approved, market and sell product candidates. If such collaborators fail to perform as expected, the potential for us to generate future revenue from such product candidates would be significantly reduced and our business would be harmed. For certain products candidates, we depend, or will depend, on our development and commercial collaborators to develop, conduct clinical trials of, and, if approved, commercialize product candidates. **Under 81** ~~Under~~ our collaborations with Genentech, Ionis, Novartis, 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. ~~---~~ **In addition, Cancer Research UK is sponsoring and funding a Phase I/ IIa clinical trial of BT1718, in patients with advanced solid tumors, and will sponsor**

and fund development of BT7401 from current preclinical studies through the completion of a Phase IIa trial in patients with advanced solid tumors. We depend on these collaborators to develop and, where applicable, commercialize products based on Bicycle peptides, and the success of their efforts directly impacts the milestones and royalties we will receive. We cannot provide assurance that our collaborators will be successful in or that they will devote sufficient resources to the development or commercialization of their products. If our current or future collaboration and commercialization partners do not perform in the manner we expect or fail to fulfill their responsibilities in a timely manner, or at all, if our agreements with them terminate or if the quality or accuracy of the clinical data they obtain is compromised, the clinical development, regulatory approval and commercialization efforts related to their and our product candidates and products could be delayed or terminated and it could become necessary for us to assume the responsibility at our own expense for the clinical development of such product candidates. Our current collaborations and any future collaborations that we enter into are subject to numerous risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to the collaborations;
- collaborators may not perform their obligations as expected or fail to fulfill their responsibilities in a timely manner, or at all;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay preclinical studies or clinical trials, provide insufficient funding for clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our shareholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- the collaborations may not result in product candidates to develop and / or preclinical studies or clinical trials conducted as part of the collaborations may not be successful;
- product candidates developed with collaborators may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to stop commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;
- public health crises and other adverse global economic events 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 Pepsan Systems B. V., and its affiliates, or Pepsan, related to a non- exclusive patent license agreement that our subsidiary, BicycleRD Limited, or BicycleRD, entered into with Pepsan 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. For example, Cancer Research UK currently sponsors and funds the Phase I/IIa clinical trial of BT1718 in patients

with advanced solid tumors. We also ~~84utilize~~ **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 these~~ **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~~ **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~~ **sponsored** trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator- sponsored trials. If so, the FDA or EMA may require us to obtain and submit additional preclinical, manufacturing, or clinical data. We intend to rely on third parties to manufacture product candidates, which increases the risk that we will not have sufficient quantities of such product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of the product candidates that we are developing or evaluating in our development programs. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We rely on third parties, 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, 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. 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 the ongoing wars involving Ukraine and Israel. 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~~ **85** ~~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; ~~86~~ • 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 ~~BT8009, zelenectide pevedotin and BT5528, and BT1718~~ use toxins or other substances that can be produced only in specialized facilities with specific authorizations and permits, and there can be no guarantee that we or our manufacturers can maintain such authorizations and permits. These specialized requirements may also limit the number of potential manufacturers that we can engage to produce our product candidates ~~and~~ impair any efforts to transition to replacement manufacturers. Our future product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP requirements that might be capable of manufacturing for us. If the third parties that we engage to supply any materials or manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, 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~~ **86** ~~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 ~~87~~ ~~our~~ ~~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 ~~88~~ **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.

~~88~~ **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. 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. Changes in either the patent laws or the interpretation of the patent laws in the United States or other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy- Smith America Invents Act, or the Leahy- Smith Act, was signed into law. When implemented, the Leahy- Smith Act included several significant changes to U. S. patent law that impacted how patent rights could be prosecuted, enforced and defended. In particular, the Leahy- Smith Act also included provisions that switched the United States from a “ first- to- invent ” system to a “ first- to- file ” system, allowed third- party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first- to- file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed new regulations and procedures governing the administration of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy- Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. It remains unclear what, if any, impact the Leahy- Smith Act will have on the operation of our business. However, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business. In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent rulings from the U. S. Court of Appeals for the Federal Circuit and the U. S. Supreme Court have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U. S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future. We cannot provide assurance that our efforts to seek patent protection for one or more of our products and product candidates will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact courts’ decisions in historical and future cases may have on the ability of life science companies to obtain or enforce patents relating to their products in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent rights and our ability to protect and enforce our intellectual property in the future. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting, maintaining, defending and enforcing patents on products and product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. There can be no assurance that we will obtain or maintain patent rights in or outside the United States under any future license agreements. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we pursue patent protection, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing

countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Proceedings to enforce our patent rights, even if obtained, in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. While we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop. ~~If~~ **91** ~~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 ~~92~~ ~~candidates~~ ~~--~~ **92** ~~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 Pepsican, 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~~ **92** ~~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 ~~93awarded~~ **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~~ **93We** 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 ~~94right~~ **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~~ **EU** European Union 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 GrowthOur 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~~ **94among** numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials may make it more challenging to recruit and retain qualified personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited. The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

~~95Our~~ **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 have recently expanded our organization significantly and we expect to continue to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We have recently experienced significant growth in the number of our employees and the scope of our operations and expect to continue 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 attention to managing these growth activities. Moreover, our expected growth could require us to relocate to geographic areas beyond those where we have been historically located. For example, we maintain office and laboratory space in Cambridge, U. K. and in Massachusetts, U. S. Due to our limited resources, we may not be able to ~~effectively~~ **95effectively** manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

~~96Risks~~ **Risks** Related to Ownership of Our Securities The market price of our ADSs is highly volatile, and holders of our ADSs may not be able to resell their ADSs at or above the price at which they purchased their ADSs. The market price of our ADSs is highly volatile. Since our initial public offering, or IPO, in May 2019, through February ~~15-20~~ **2024-2025**, the trading price of our ADSs has ranged from \$ 6. 24 to \$ 62. 08. The stock market in general, and the market for ~~biopharmaceutical~~ **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; **96** • 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; **97** • 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, the ongoing wars involving Ukraine and Israel have created extreme volatility in the global capital markets and **is-are** expected to have further global economic consequences, including 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 can adversely affect us by increasing our costs, including labor and employee benefit costs. In addition, higher inflation and macro turmoil and uncertainty could also adversely affect our buyers and sellers, which could reduce demand for our products. 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 February **15-20, 2024-2025**, we had **37-47, 880-710, 303-256** ordinary shares, nominal value £ 0. 01 per share, and **4-21, 705-492, 882-099** 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 **as summarized in Exhibit 4-6, as filed with this Annual Report**. 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 - **Consequently, if holders of our- or upon at least 61 days’ notice, not in excess of 19. 9 % . Any re- designation of** non- voting ordinary shares **as ordinary shares** exercise their option to make this re- designation, this 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 For example, 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 to (assuming, for these purposes, that the they extent permitted, were able to do so in compliance with the prior beneficial ownership limitation), based on the number of ordinary shares and non- voting ordinary shares outstanding on December 31, 2024, the ordinary shares outstanding prior to the re- designation would have approximately 69 90.01% of the voting power - and the former non- voting ordinary shares would represent approximately 31 9.99% of the voting power. 97Substantial Future sales, or the possibility of future sales, of a substantial number of our- 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 our- or ADSs in, and sales by our management, our directors, the their public market affiliates, or significant shareholders, could occur at any time . In June 2024, subject to we registered for resale 37, 656, 764 ordinary shares, representing 37, 656, 764 ADSs that were or may become beneficially owned by selling securityholders, including certain restrictions described below entities affiliated with Baker Bros . If Advisors LP, our- or existing shareholders sell, or indicate the Baker Entities. The selling securityholders will determine whether an- and when these intent to sell, substantial amounts of our securities are resold in the public market, the trading price. These shares represent a large number of our ordinary shares, and if sold in the market in transactions that occur at about the same time, such transactions could depress the market of our ADSs and could decline significantly and could decline below also affect our ability to raise equity capital through the sale current trading prices 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. Based on information available to us, the Baker Entities beneficially own approximately 22.9 % of our ordinary shares. 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, a member 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 59 % of our voting power as of February 20, 2025. 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.**

~~98Because~~ **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. ~~In addition, the terms of our indebtedness with Hercules prohibit us from paying dividends.~~ 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-98Risks** 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 United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U. S. securities laws, would not automatically be recognized or enforceable in the United Kingdom. In addition, uncertainty exists as to whether U. K. courts would entertain original actions brought in the United Kingdom against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U. S. courts would be treated by the courts of the United Kingdom as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U. S. securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision. If an English court gives judgment for the sum payable under a U. S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. As a result, U. S. investors may not be able to enforce against us or our senior management, board of directors or certain experts named herein who are residents of the United Kingdom or countries other than the United States any judgments obtained in U. S. courts in civil and commercial matters, including judgments under the U. S. federal securities laws. If we are a controlled foreign corporation, there could be adverse U. S. federal income tax consequences to certain U. S. holders. Each "Ten Percent Shareholder" (as defined below) in a non-U. S. corporation that is classified as a "controlled foreign corporation," or a CFC, for U. S. federal income tax purposes generally is required to report annually and include in income for U. S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income," "global intangible low-taxed income," and investment of earnings in U. S. property, even if the CFC has made no distributions to its shareholders. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. An individual that is a Ten Percent Shareholder with respect to a CFC generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a U. S. corporation that is a Ten Percent Shareholder with respect to a CFC. Failure to comply with these reporting and tax paying obligations may subject a Ten Percent Shareholder to ~~99significant~~ **significant** monetary penalties and may prevent the statute of limitations from starting with respect to such shareholder's U. S. federal income tax return for the year for which reporting was due. A non-U. S. corporation generally will be classified as a CFC for U. S. federal income tax purposes if Ten Percent Shareholders own (directly, indirectly or constructively through the application of attribution rules) more than 50 % of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own (directly, indirectly or constructively through the application of attribution rules) 10 % or more of the total combined voting power of all

classes of stock entitled to vote or 10 % or more of the total value of all classes of stock of such corporation. Each Ten Percent Shareholder should also be aware that because our group includes a U. S. subsidiary, certain of our non- U. S. subsidiaries will be treated as CFCs (regardless of whether or not we are treated as a CFC). We cannot provide any assurances that we will assist shareholders in determining whether we are or any of our non- U. S. subsidiaries is ~~treated as~~ **99treated** as a CFC or whether any shareholder is treated as a Ten Percent Shareholder with respect to any such CFC or furnish to any shareholders information that may be necessary to comply with reporting and tax paying obligations. The Internal Revenue Service has provided limited guidance on situations in which investors may rely on publicly available information to comply with their reporting and tax paying obligations with respect to foreign- controlled CFCs. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. United States persons should consult their own tax advisors with respect to the potential adverse U. S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are a 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 ~~not~~ **2023-2024** a PFIC in the ~~2023-2024~~ **2024** taxable year. ~~However~~ **In addition**, no assurances can be provided that we will not be a PFIC ~~the current or~~ **the current or** 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, or QEF, 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 United Kingdom, 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 ~~100for~~ **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 ~~relief program, being the~~ **credit regime. In respect of accounting periods in which we qualify as a** Small and Medium- sized Enterprises ~~Enterprise, or SME, and in which our relevant~~ **R & D Tax Relief program, or SME Program, and for certain specific categories of expenditure represents 40 % (** the Research and Development Expenditure Credit program, or RDEC Program. The SME Program may be particularly beneficial to us, as under such program the trading losses that arise from our qualifying R & D activities can be surrendered for a cash rebate of up to 33. 35 % of qualifying expenditure incurred prior to April 1, 2023 ~~2024~~ **2024**, 30 % and up to 18. 6 %) **or more of qualifying** ~~the total relevant~~ **expenditure** incurred thereafter. Amendments to the U. K. R & D tax credit regime that are contained in the Finance Bill currently proceeding through the U. K. Parliament will ~~(meaning if enacted) increase the cash rebate that may be claimed from such date to 26. 97 % of qualifying expenditure, if we also qualify as “ R & D intensive ” for an~~ **during such** accounting period) ~~(broadly, a we may, under this regime, surrender the trading loss losses making SME whose that arise from our R & D activities for a cash rebate of up to 26. 97 % of qualifying R & D expenditure represents 40 % (or, from April 1, 2024, 30 %) or more of its total expenditure for that accounting period).~~ **Accordingly,** These amendments will also ~~(if enacted) with effect from April 1, 2024 (i) unless limited exceptions apply, introduce restrictions on the tax relief that can be claimed for expenditure 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, and (ii) merge the SME Program and the RDEC Program into a single scheme. If such proposals are implemented as currently provided in the Finance Bill, and we do not 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 ~~such cash rebates~~ **payments or other tax relief (under other provisions of the U. K. R & D tax credit regime)** at a significantly lower rate than ~~we can claim~~ at present. ~~These and~~ **Further, other** ~~--~~ **the potential regime’ s rules are complex, and if a tax authority were to challenge or seek to disallow our claims (in whole 100or 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 ~~relief programs~~ **credit regime** may mean ~~that~~ **that** we no longer qualify ~~for it~~ **for it** or have a material impact on the extent to which we can make claims ~~(or benefit from them)~~ **(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 (which may change, in particular, if the Finance Bill currently proceeding through the U. K. Parliament is not enacted in its current form, or if measures taken to give certain Finance Bill provisions effect on a provisional basis do not continue to apply until such enactment). In the United States on August 16, 2022, President Biden signed into law the IRA, which 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, beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminated the option to deduct research and development expenditures and requires taxpayers to capitalize and subsequently amortize such expenses over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. Although Congress is considering legislation that would defer the amortization requirement to later ~~101 years~~ **years**, we have no assurance that the provision will be repealed or otherwise modified. If the requirement is not modified or deferred, it may materially reduce our cash flows. 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~~ **101 liabilities**, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable. Provisions in the U. K. City Code on Takeovers and Mergers that may have anti- takeover effects do not apply to us. The U. K. City Code on Takeovers and Mergers, or the Takeover Code, applies to an offer for, among other things, a public company whose registered office is in the United Kingdom if the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom (or the Channel Islands or the Isle of Man). This is known as the “ residency test. ” The test for central management and control under the Takeover Code is different from that used by the U. K. tax authorities. Under the Takeover Code, the Takeover Panel will determine whether we have our place of central management and control in the United Kingdom by looking at various factors, primarily where the directors are resident. In September 2019, the Takeover Panel Executive confirmed that, based on our current circumstances, we are not subject to the Takeover Code. As a result, our shareholders are not entitled to the benefit of certain takeover offer protections provided under the Takeover Code. We believe that this position is unlikely to change at any time in the near future but, in accordance with good practice, we will review the situation on a regular basis and consult with the Takeover Panel if there is any change in our circumstances which may have a bearing on whether the Takeover Panel would determine our place of central management and control to be in the United Kingdom. The rights of our shareholders may differ from the rights typically offered to shareholders of a U. S. corporation. We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the U. K. Companies Act 2006, or the Companies Act, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U. S. corporations. The principal differences include the following: ● under English law and our articles of association, each shareholder present at a meeting has only one vote unless demand is made for a vote on a poll, in which case each holder gets one vote per share owned. Under U. S. law, each shareholder typically is entitled to one vote per share at all meetings; ● under English law, the number of shares determines the number of votes a holder may cast only on a poll. However, that the voting

rights of ADSs are also governed by the provisions of a deposit agreement with our depository bank; ~~102~~ 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~~ **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; ~~and~~ the quorum requirement for a shareholders’ meeting is a minimum of two shareholders entitled to vote at the meeting and present in person or by proxy or, in the case of a shareholder that is a corporation, represented by a duly authorized officer. Under U. S. law, a majority of the shares eligible to vote must generally be present (in person or by proxy) at a shareholders’ meeting in order to constitute a quorum. The minimum number of shares required for a quorum can be reduced pursuant to a provision in a company’s certificate of incorporation or bylaws, but typically not below one-third of the shares entitled to vote at the meeting.

~~103~~ **General Risks** Effective as of December 31, 2023, we are a large accelerated filer, which may increase our costs and demands on management. As a result of the market value of our ordinary shares and ADSs held by non-affiliates as of June 30, 2023, we are a large accelerated filer as of December 31, 2023 and no longer qualify as a “smaller reporting company” as defined in the Exchange Act. However, we are not required to reflect the change in our smaller reporting company status and comply with the associated increased disclosure obligations until our first quarterly report for the three-month period ending March 31, 2024. As a large accelerated filer, we are subject to certain disclosure and compliance requirements that apply to other public companies. These requirements include, but are not limited to: the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404 (b) of the Sarbanes-Oxley Act of 2002; compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements; and the requirement that we provide full and more detailed disclosures regarding executive compensation. Compliance with the additional requirements of being a large accelerated filer may increase our legal and financial compliance costs and may cause management and other personnel to divert attention from operational and other business matters to devote increased time to public company reporting requirements. In addition, if we are not able to comply with the changing requirements in a timely manner, the market price of our ADSs could decline, and we could be subject to sanctioning or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources. 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 ~~at such time when we are no longer a smaller reporting company~~. 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, ~~104~~ **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~~ **103coverage** 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. ~~105~~ **104**