Risk Factors Comparison 2024-02-22 to 2023-02-28 Form: 10-K

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You should carefully consider the risks described below, together with all of the other information included in this Form 10- K, in considering our business and prospects. Set forth below and elsewhere in this Form 10- K and in other documents we file with the SEC are descriptions of certain risks, uncertainties, and other factors that could cause our actual results to differ materially from those anticipated. If any of the following risks, other unknown risks, or risks that we think are immaterial occur, our business, financial condition, results of operations, cash flows, or growth prospects could be adversely impacted, in which case, the market price of our ordinary shares could decline, and you may lose all or part of your investment in our ordinary shares. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Risks Relating to Our Financial Position, Our Need for Additional Capital, and Our Business We anticipate that we will incur losses for the foreseeable future and we may never sustain profitability. We may not generate the cash that is necessary to finance our operations in the foreseeable future. We incurred net income (losses) of $ (**147. 0) million, $ (** 116. 9) million ~~,~~ **and** $ 67. 0 ~~million and $ (111. 1)~~ million for the years ended December 31, **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~, respectively. As of December 31, ~~2022~~ **2023**, we had an accumulated deficit of $ ~~833~~ **(980** . 0 **)** million. We expect to continue to incur substantial losses for the foreseeable future as we: • support the Phase 3 AFFIRM- AL clinical trial for birtamimab, the Phase 1 clinical ~~trial~~ **trials** ~~for PRX005, the Phase 1 clinical trial~~ for PRX012, and potential additional clinical trials for these and other programs **, including PRX123** ; • develop and possibly commercialize our drug candidates, including birtamimab ~~, prasinezumab, PRX005~~ , PRX012, and PRX123; • undertake nonclinical development of other drug candidates and initiate clinical trials, if supported by nonclinical data; • pursue our early stage research and seek to identify additional drug candidates; and • potentially acquire rights from third parties to drug candidates or technologies through licenses, acquisitions, or other means. We must generate significant revenue to achieve and maintain profitability. Even if we succeed in discovering, developing, and commercializing one or more drug candidates, we may not be able to generate sufficient revenue and we may never be able to achieve or sustain profitability. We will require additional capital to fund our operations, and if we are unable to obtain such capital, we will be unable to successfully develop and commercialize drug candidates. As of December 31, ~~2022~~ **2023** , we had cash and cash equivalents of $ ~~710~~ **618** . ~~4~~ **8** million **. The majority of such cash is held in accounts at U. S. banking institutions that we believe are of high quality. Cash held in depository accounts may exceed the $ 250, 000 Federal Deposit Insurance Corporation insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations** . Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in order to continue the research and development, and eventual commercialization, of our drug candidates. Our future capital requirements will depend on many factors that are currently unknown to us, including, without limitation: • the timing of progress, results, and costs of our clinical trials, including the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab being conducted by Roche, the Phase 2b clinical trial for prasinezumab being conducted by Roche, the Phase 2 clinical trial for NNC6019 (formerly PRX004) being conducted by Novo Nordisk, the Phase 1 clinical trial for **BMS- 986446 (formerly** PRX005 **) being conducted by BMS** , and the Phase 1 clinical ~~trial~~ **trials** for PRX012; • the timing, initiation, progress, results, and costs of these and our other research, development, and possible commercialization activities; • the results of our research ~~and~~ **,** nonclinical **studies,** and clinical ~~studies~~ **trials** ; • the costs of manufacturing our drug candidates for clinical development as well as for future commercialization needs; • if and when appropriate, the costs of preparing for commercialization of our drug candidates; • the costs of preparing, filing, and prosecuting patent applications, and maintaining, enforcing, and defending intellectual property- related claims; • our ability to establish strategic collaborations, licensing, or other arrangements; • the timing, receipt, and amount of any capital investments, cost- sharing contributions or reimbursements, milestone payments, or royalties that we might receive under current or potential future collaborations; • the costs to satisfy our obligations under current and potential future collaborations; and • the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates. We have based our expectations relating to liquidity and capital resources on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development and commercialization of our current drug candidates. In the pharmaceutical industry, the research and development process is lengthy and involves a high degree of risk and uncertainty. This process is conducted in various stages and, during each stage, there is substantial risk that drug candidates in our research and development pipeline will experience difficulties, delays or failures. This makes it difficult to estimate the total costs to complete our clinical trials and to estimate anticipated completion dates with any degree of accuracy, which raises concerns that attempts to quantify costs and provide estimates of timing may be misleading by implying a greater degree of certainty than actually exists. In order to develop and obtain regulatory approval for our drug candidates we will need to raise substantial additional funds. We expect to raise any such additional funds through public or private equity or debt financings, collaborative agreements with corporate partners, or other arrangements. Our ability to raise additional capital, including our ability to secure new collaborations, may also be adversely impacted by global economic conditions ~~and the recent~~ **, including any** disruptions to, and volatility in, the credit and financial markets in the United States and worldwide **,** ~~resulting from the ongoing COVID- 19 pandemic and~~ geopolitical turmoil, ~~including~~ **and the ongoing conflict in Israel and any potential escalation or geographic**

expansion of such conflict, which could heighten ~~the~~ **other** ~~Russian invasion of Ukraine~~ **risks identified in this report** . We cannot assure that additional funds will be available when we need them on terms that are acceptable to us or at all. If we raise additional funds by issuing equity securities, including pursuant to our December 2021 Distribution Agreement (**as may be amended from time to time, and** as discussed below), substantial dilution to existing shareholders would result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business. We may be required to relinquish rights to our technologies or drug candidates or grant licenses on terms that are not favorable to us in order to raise additional funds through strategic alliances, joint ventures, or licensing arrangements. If adequate funds are not available on a timely basis, we may be required to: • terminate or delay clinical trials or other development activities for one or more of our drug candidates; • delay arrangements for activities that may be necessary to commercialize our drug candidates; • curtail or eliminate our drug research and development programs that are designed to identify new drug candidates; or • cease operations. In addition, if we do not meet our payment obligations to third parties as they come due, we may be subject to litigation claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and distract management and may have unfavorable results that could further adversely impact our financial condition ~~. The United Kingdom' s withdrawal from the European Union could have a negative effect on global economic conditions and financial markets, European Union regulatory procedures and our business. Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the European Union (" EU ") on January 31, 2020, commonly referred to as Brexit. The United Kingdom remained in the EU customs union and the single market for a transition period which expired on December 31, 2020. On December 24, 2020, the United Kingdom and the EU reached agreement in principle on their future trading relationship and entered into the EU- UK Trade and Cooperation Agreement which was formally ratified by the parties and as of May 1, 2021, is fully in force. However, because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the EU as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains as to aspects of the future relationship between the United Kingdom and the EU. The uncertainty surrounding Brexit has had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict access to capital, which could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects~~ . Our future success depends on our ability to retain key personnel and to attract, retain, and motivate qualified personnel. We are highly dependent on key personnel, including Dr. Gene G. Kinney, our President and Chief Executive Officer. There can be no assurance that we will be able to retain Dr. Kinney or any of our key personnel. The loss of the services of Dr. Kinney or any other person on whom we are highly dependent might impede the achievement of our research, development, and commercial objectives. We do not carry " key person " insurance covering any members of our senior management. Attracting and retaining qualified scientific and other personnel are critical to our growth and future success. Competition for qualified personnel in our industry is intense. We may not be able to attract and retain these personnel on acceptable terms given that competition. Additionally, we may not be able to integrate and motivate qualified personnel to enable them to succeed in their positions. Failure to attract, integrate, retain, and motivate qualified personnel could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects. Our collaborators, prospective collaborators, and suppliers may need assurances that our financial resources and stability on a stand- alone basis are sufficient to satisfy their requirements for doing or continuing to do business with us. Some of our collaborators, prospective collaborators, and suppliers may need assurances that our financial resources and stability on a stand- alone basis are sufficient to satisfy their requirements for doing or continuing to do business with us. If our collaborators, prospective collaborators or suppliers are not satisfied with our financial resources and stability, it could have a material adverse effect on our ability to develop our drug candidates, enter into licenses or other agreements and on our business, financial condition or results of operations. The agreements we entered into with Elan involve conflicts of interest and therefore may have materially disadvantageous terms to us. We entered into certain agreements with Elan in connection with our separation from Elan, which set forth the main terms of the separation and provided a framework for our initial relationship with Elan. These agreements may have terms that are materially disadvantageous to us or are otherwise not as favorable as those that might be negotiated between unaffiliated third parties. In December 2013, Elan was acquired by Perrigo Company plc (" Perrigo "), and in February 2014 Perrigo caused Elan to sell all of its shares of Prothena in an underwritten offering. As a result of the acquisition of Elan by Perrigo and the subsequent sale of all of its shares of Prothena, Perrigo may be less willing to collaborate with us in connection with the agreements to which we and Elan are a party and other matters. We **have been, and** may **in the future** be **,** adversely affected by **business disruptions beyond our control, including outbreaks of epidemic, pandemic, or contagious disease, geopolitical turmoil,** earthquakes ~~,~~ **or other** natural disasters, and adverse weather events, including as a result of climate change. **The operational and financial impact of a business disruption beyond our control, such as a public health crisis, geopolitical turmoil, or an adverse weather event has, and could, adversely affect our business in the following ways: • As we have seen with the outbreak of the COVID- 19 pandemic, outbreaks of epidemic, pandemic, or contagious disease or other public health emergencies have historically and may in the future disrupt our operations, including clinical trials, research and nonclinical studies, the manufacture or shipment of both drug substance and finished drug product for drug candidates for preclinical testing and clinical trials, and access to stable credit and financial markets in the United States and worldwide. For example, the Phase 3 clinical trial for birtamimab and the Phase 2 clinical trial for prasinezumab conducted by Roche were disrupted by the COVID- 19 pandemic as a result of (i) the inability or unwillingness of study participants, site investigators or other study personnel to travel to clinical trial sites or otherwise follow study protocols and (ii) the diversion of healthcare resources away from the conduct of clinical**

trials. • Geographic regions where we operate may be affected by war, terrorism, or political instability, and our operations may be vulnerable to disruption, including disturbances to the credit and financial markets (in such region or worldwide), or to services generally, including healthcare services. For example, the Phase 3 clinical trial for birtamimab has clinical trial sites located globally, including in Israel and Eastern Europe, and operations at such clinical trial sites may be disrupted by ongoing conflicts and / or new conflicts, which could result in (i) the inability or unwillingness of study participants, site investigators or other study personnel to travel to such clinical trial sites or otherwise follow study protocols, (ii) the diversion of healthcare resources away from the conduct of clinical trials, or (iii) the complete or partial cessation of operations at such clinical trial sites. • Our key **research** facility and ~~most~~ **a significant portion** of our operations are in the San Francisco Bay Area of Northern California, which in the past has experienced severe earthquakes. If an earthquake, other natural disaster, or similar event were to occur and prevent us from using all or a significant portion of those operations or local critical infrastructure, or that otherwise disrupts our operations, it could be difficult or impossible for us to continue our business for a substantial period of time. We have disaster recovery and business continuity plans, but they may prove to be inadequate in the event of a natural disaster or similar event. We may incur substantial expenses if our disaster recovery and business continuity plans prove to be inadequate. We do not carry earthquake insurance. Furthermore, third parties upon which we are materially dependent upon **, including our clinical trial sites,** may be vulnerable to natural disasters or similar events. **•** Climate change could have an impact on longer- term natural weather trends. Extreme weather events that are linked to rising temperatures, changing global weather patterns, sea, land and air temperatures, as well as sea levels, rain and snow could result in increased occurrence and severity of adverse weather events. Any ~~, such adverse weather~~ **one or more of these force majeure** ~~event~~ **events** ~~, natural disaster or similar occurrence~~ could have ~~an~~ **a material** adverse effect on our ~~business~~ **liquidity, results of operations** , financial condition **or business** , **including the progress of, and timelines** ~~or~~ **for** ~~results~~ **, our nonclinical and clinical development programs, and may create safety challenges for our employees and safe occupancy** of **our job sites, financial market volatility and significant macroeconomic uncertainty in global markets. Furthermore, any governmental or business actions, or any actions taken by individuals in response to any such events (including mandatory quarantines, travel restrictions, delay in** operations **of the U. S. FDA and comparable foreign regulatory agency, and interruptions to healthcare services), may divert healthcare resources away from the conduct of clinical trials and development programs** . We may experience breaches or similar disruptions of our information technology systems or data. Our business is increasingly dependent on critical, complex, and interdependent information technology systems to support business processes as well as internal and external communications. Despite the implementation of security measures, our internal computer systems, and those of our current and any future CROs and other contractors, consultants, and collaborators, ~~are~~ **have been subject to and remain** vulnerable to damage from cyberattacks, " phishing " attacks, ransomware, computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication or electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication, and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID- 19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to or to sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Any breakdown, malicious intrusion, or computer virus could result in the impairment of key business processes or breach of data security, which could result in a material disruption of our development programs and cause interruptions in our business operations, whether due to a loss of our trade secrets or other intellectual property or lead to unauthorized disclosure of personal data of our employees, third parties with which we do business, clinical trial participants, or others. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, such a breach may require notification to governmental agencies, the media, or individuals pursuant to applicable data privacy and security law and regulations. Such an event could have an adverse effect on our business, financial condition, or results of operations. Changes in and failures to comply with U. S. and foreign privacy and data protection laws, regulations, and standards may adversely affect our business, operations, and financial performance. We and our partners **are** ~~may be~~ subject to **certain** federal, state, and foreign data privacy and security laws and regulations. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and may increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations, including state security breach notification laws, federal and state health information privacy laws (including U. S. Health Insurance Portability and Accountability Act of 1996 (" HIPAA "), as amended by the Health Information Technology for Economic and Clinical Health Act, and regulations promulgated thereunder), and federal and state consumer protection laws **(including Section 5 of the Federal Trade Commission Act)** , govern the collection, use, disclosure, and protection of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues **. State privacy laws in particular are evolving, with more than a dozen new state privacy laws passed in recent years, along with additional health privacy specific laws. These laws may further increase our compliance obligations, and potential legal privacy risks. For example, Washington recently passed the My Health My Data Act, which has a broader scope than HIPAA and includes a private right of action. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and the regulations promulgated thereunder. Depending on the facts and circumstances, we**

could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA. Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time- intensive process, and we may be required to substantially amend existing procedures and policies or put in place additional procedures and policies to ensure compliance with privacy and data protection rules and requirements. These changes could adversely impact our business by increasing operational and compliance costs or impact business practices. Further, there is a risk that the amended policies and procedures will not be implemented correctly or that individuals within the business will not be fully compliant with the new procedures. If we fail to comply with any such laws or regulations, we may face significant litigation, government investigations, fines and penalties as well as reputational damage which could adversely affect our business, operations, financial condition and prospects. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements . For example, the California Consumer Privacy Act (the " CCPA ") went into effect January 1, 2020. The CCPA, among other things, imposes new data privacy obligations on covered companies and provides expanded privacy rights to California residents, including the right to access, delete, and opt out of certain disclosures of their information. The CCPA provides for civil penalties for violations, as well as a private right of action with statutory damages for certain data breaches, which may increase the frequency and likelihood of data breach litigation. Although the law includes limited exceptions for health- related information, including clinical trial data, such exceptions may not apply to all of our operations and processing activities. Further, the California Privacy Rights Act (the " CPRA ") ~~recently passed in California. The CPRA will impose~~ **imposes** additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, ~~new~~ audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It ~~will~~ also ~~create~~ **creates** a ~~new~~ California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions **went** ~~will go~~ into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. **Although** ~~In addition,~~ the CCPA **currently exempts certain health- related information, including clinical trial data, the CCPA and the amendments under the CPRA may increase our compliance costs and potential liability. Multiple states have followed California to legislate comprehensive privacy laws with data privacy rights. For example, Virginia passed the Virginia Consumer Data Protection Act, which went into effect on January 1, 2023 and affords consumers similar rights to the CCPA, along with additional rights, such** ~~has~~ **as** ~~prompted a number~~ **the right to opt- out** of ~~proposals~~ **processing** for **profiling and targeted advertising purposes. Additionally, the Colorado Privacy Act and Connecticut Personal Data Privacy and Online Monitoring Act went into effect on July 1, 2023. While these** new **laws generally include exemptions for HIPAA- covered and clinical trial data, they impact the overall privacy landscape. Several other states have followed suit and passed similar legislation which will go into effect in the coming years. Further, additional privacy laws that are similar in nature have been proposed in other states and at the** federal **level** and ~~state privacy legislation that~~ , if passed, ~~could increase our~~ **such laws may have** ~~potential~~ **potentially** ~~liability, increase our~~ **conflicting requirements that would make** compliance **challenging** ~~costs and adversely affect our business. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or applicable state laws~~ . We are also or may become subject to rapidly evolving data protection laws, rules, and regulations in foreign jurisdictions. For example, **in** the European Union **(" EU "), the EU** General Data Protection Regulation (the " EU GDPR ") governs the collection of, and other processing activities involving, personal data (i. e., data which identifies an individual or from which an individual is identifiable) **,** including ~~,~~ clinical trial data, and grants individuals various data protection rights (e. g., the right to **the** erasure of personal data). The EU GDPR imposes a number of obligations on companies, including inter alia: (i) accountability and transparency requirements, and enhanced requirements for obtaining valid consent; (ii) ~~obligations~~ **obligation** to consider data protection ~~as~~ **when** any new products or services are developed **,** and to limit the amount of personal data processed; and (iii) obligations to implement appropriate technical and organizational measures to safeguard personal data and to report certain personal data breaches to **: (x)** the **data protection** supervisory authority without undue delay (and no later than 72 hours **,** where feasible) **after becoming aware of the personal data breach, unless the personal data breach is unlikely to result in a risk to the data subjects' rights and freedoms; and (y) affected data subjects where the personal data breach is likely to result in a high risk to their rights and freedoms** . In addition, the EU GDPR prohibits the transfer of personal data from the European Economic Area (" EEA ") to ~~the United States and other~~ jurisdictions that the European Commission does not recognize as having " adequate " data protection laws unless a data transfer mechanism has been put in place **or a derogation under the EU GDPR can be relied on** . In July 2020, the Court of Justice of the **EU** ~~European Union~~ limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU- US Privacy Shield **Framework** for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (" **EU** SCCs ") including, a requirement for companies to carry out a transfer privacy impact assessment **(" TIA ")** , which **,** among other things, assesses the laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under the **EU** SCCs will need to be implemented to ensure an **"** essentially equivalent **"** level of data protection to that afforded in the EEA **. On July 31, 2023, the European Commission adopted its Final Implementing Decision granting the United States adequacy (" Adequacy Decision "), for EU- U. S. transfers of personal data for entities self- certified to the EU- U. S. Data Privacy Framework (" DPF "). Entities relying on EU SCCs for transfers to the United States are also able to rely on the analysis in the Adequacy Decision as support for their TIA regarding the equivalence of U. S. national security safeguards and redress** . The EU GDPR imposes substantial fines for breaches and violations (up to the greater of € 20 million or 4 % of ~~our~~ **the**

noncompliant company' s total annual global ~~revenue~~ **turnover**). The EU GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with **data protection** supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the EU GDPR. **The** ~~Relatedly, following the United Kingdom' s withdrawal from the EU (i. e., Brexit), and the expiry of the Brexit transition period, which ended on December 31, 2020, the~~ EU GDPR has been implemented **(as implemented, the " UK GDPR ")** in the United Kingdom (~~as the~~ " UK ~~GDPR~~ "). The UK GDPR sits alongside the UK Data Protection Act 2018 which implements certain derogations in the EU GDPR into UK law. Under the UK GDPR, companies not established in the UK but ~~who~~ **which** process personal data in relation to the offering of goods or services to individuals in the UK, or ~~to~~ **the** ~~monitor~~ **monitoring of** their behavior will be subject to the UK GDPR – the requirements of which are (at this time) largely aligned with those under the EU GDPR and as such, may lead to similar compliance and operational costs with potential fines up to the greater of £ 17. 5 million or 4 % of **the noncompliant company' s total annual** global turnover **. The UK GDPR also imposes similar restrictions on international transfers of personal data from the UK to jurisdictions that the UK Government does not consider " adequate ". The UK' s Information Commissioner' s Office published: (i) its own form of EU SCCs, known as the International Data Transfer Agreement for transfers to outside the UK; (ii) a " UK addendum " to the new EU SCCs which amends the relevant provisions of such clauses to work in a UK context; and (iii) its own version of the TIA (although entities may choose to adopt either the EU or UK- style TIA). Further, on September 21, 2023, the UK Secretary of State for Science, Innovation and Technology established a UK- U. S. data bridge (i. e., a UK equivalent of the Adequacy Decision) and adopted UK regulations to implement the UK- U. S. data bridge (" UK Adequacy Regulations "). Personal data may now be transferred from the UK under the UK- U. S. data bridge through the UK extension to the DPF to organizations self- certified under the UK extension to the DPF** . The above- described changes **may** lead to additional costs and increase our overall risk exposure. Compliance with U. S. and foreign data privacy and security laws, rules, and regulations ~~could~~ **have required us, and may** require us **in the future,** to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. If we fail to comply with any such laws, rules, or regulations, we may face government investigations and / or enforcement actions, fines, civil or criminal penalties, private litigation, or adverse publicity that could adversely affect our business, financial condition, and results of operations ~~. The COVID- 19 pandemic has adversely affected our business and could have a material adverse effect on our liquidity, results of operations, financial condition or business, including our nonclinical and clinical development programs. The outbreak of the novel strain of coronavirus SARS- CoV- 2, which causes coronavirus disease (" COVID- 19 "), continues to be a global pandemic. While it is not possible at this time to estimate the overall impact that COVID- 19 could have on our business, the continued rapid spread of COVID- 19, the emergence of variant strains, and the measures taken by the governments and local authorities of affected countries and local jurisdictions, has disrupted our Phase 2 clinical trial for prasinezumab, has delayed initiating clinical trial sites for our Phase 3 clinical trial for birtamimab, and could disrupt and delay our planned clinical trials, our research and nonclinical studies, the manufacture or shipment of both drug substance and finished drug product for our drug candidates for preclinical testing and clinical trials and materially adversely impact our liquidity, results of operations, financial condition, or business, including the following: • our Phase 2 clinical trial for prasinezumab has been disrupted and this and other clinical trials pursued by us and our collaboration partners may be further delayed or interrupted, including as a result of (i) interruptions of supply to clinical trial sites of drug candidate or other equipment or materials, (ii) inability or unwillingness of site investigators or other study personnel to travel to study sites, dispense drug product, or otherwise treat or monitor study participants or follow study protocols, or conduct necessary data collection or verification, (iii) inability or unwillingness of study participants to travel to clinical trial sites, receive infusions, or otherwise continue to participate in the study, (iv) diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, or (v) interruptions in contracting with essential third- party vendors; • initiation of clinical trial sites for our Phase 3 clinical trial for birtamimab has been delayed and we, or our collaboration partners, may be further delayed in or prevented from initiating new clinical trials of current or prospective drug candidates because of (i) delays or difficulties in manufacturing drug product, (ii) delays or difficulties preparing regulatory submissions, (iii) delays or difficulties contracting with essential third- party vendors (such as contract research organizations), (iv) delays or difficulties enlisting site investigators or initiating clinical trial sites, (v) delays or difficulties recruiting or enrolling study participants, or (vi) delays or difficulties supplying drug product or other equipment or materials to clinical trial sites or other locations; • we may experience delays or interruptions in our business operations due to our key personnel, or a significant number of our personnel, becoming infected with COVID- 19 and therefore being unable to work, even remotely, for an extended period of time; • interruption or delays in the operations of the FDA and comparable foreign regulatory agencies may impact review, inspection, and approval timelines for any of our development programs; • the pandemic may adversely affect our collaboration partners, Roche, BMS, and / or Novo Nordisk, in ways that adversely impacts our collaborations with them; • business development opportunities may become more limited or difficult to undertake; • our costs may significantly increase to manage impacts to our business to complete our planned operations within our projected timelines; • changes in local regulations as part of a response to COVID- 19 may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or discontinuation of the clinical trials altogether; • we may experience delays in necessary interactions with local regulators, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; or • our liquidity needs may be adversely impacted by the economic effects of the pandemic on financial markets. Any one or more of these risks could have a material adverse effect on our liquidity, results of operations, financial condition or business, including the progress of, and timelines for, our nonclinical and clinical development programs.**

~~In addition, the spread of COVID- 19 has caused a broad impact globally, and may materially affect us economically. For example, if the subtenant to the office space that we subleased in South San Francisco, California defaults on its payment obligations, we will not receive sublease income to offset our lease payments to the landlord of the South San Francisco office space until such time as we are able to secure a new subtenant and enter into a new sublease agreement. The spread of COVID- 19 has had a negative impact on the commercial real estate market and there can be no assurance that we would be able to re- sublet the space for the same rent that the current subtenant is obligated to pay us or at all. While the potential economic impact brought by, and the duration of, COVID- 19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID- 19 could materially affect our business and the market price of our ordinary shares~~ . Risks Related to the Discovery, Development, and Regulatory Approval of Drug Candidates Our success is largely dependent on the success of our research and development programs. Our drug candidates are in various stages of development and we may not be able to successfully discover, develop, obtain regulatory approval for, or commercialize any drug candidates. The success of our business depends substantially upon our ability to discover, develop, obtain regulatory approval for and commercialize our drug candidates successfully. Our research and development programs are prone to the significant and likely risks of failure inherent in drug development, which can result from the failure of the drug candidate to be sufficiently effective, the safety profile of the drug candidate, a clinical trial that is not sufficiently enrolled or powered or adequately designed to detect a drug effect, or other reasons. We intend to continue to invest most of our time and financial resources in our research and development programs. There is no assurance that the results of the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for NNC6019, the Phase 1 clinical trial for ~~PRX005~~ **BMS- 986446** , and the Phase 1 clinical ~~trial~~ **trials** for PRX012 will support further development of these drug candidates. In addition, we currently do not, and may never, have any other drug candidates in clinical trials, and we have not identified drug candidates for many of our research programs. Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in adequate and well- controlled clinical trials that the drug candidate is safe and effective for use for that target indication. In the U. S., this must be done to the satisfaction of the FDA; in the EU, this must be done to the satisfaction of the European Medicines Agency (the " EMA "); and in other countries this must be done to the satisfaction of comparable regulatory authorities. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. Despite our efforts, our drug candidates may not: • offer improvement over existing treatment options; • be proven safe and effective in clinical trials; or • meet applicable regulatory standards. Positive results in nonclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from early clinical trials of a drug candidate may not be replicated in later clinical trials. Interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials even after achieving promising results in early- stage development. Accordingly, the results from completed nonclinical studies and early clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage studies or trials. Our nonclinical studies or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical studies or clinical trials, or to discontinue clinical trials altogether. Furthermore, we have not marketed, distributed, or sold any products. Our success will, in addition to the factors discussed above, depend on the successful commercialization of any drug candidates that obtain regulatory approval. Successful commercialization may require: • obtaining and maintaining commercial manufacturing arrangements with third- party manufacturers; • developing the marketing and sales capabilities, internal and / or in collaboration with pharmaceutical companies or contract sales organizations, to market and sell any approved drug; and • acceptance of any approved drug in the medical community and by patients and third- party payers. Many of these factors are beyond our control. We do not expect any of our drug candidates to be commercially available for several years and some or all may never become commercially available. Accordingly, we may never generate revenues through the sale of products. We have entered into collaborations with Roche and BMS and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations. Research, development, commercialization and / or strategic collaborations, including those that we have with Roche and BMS, are subject to numerous risks, which include the following: • collaborators may have significant control or discretion in determining the efforts and resources that they will apply to a collaboration, and might not commit sufficient efforts and resources or might misapply those efforts and resources; • we may have limited influence or control over the approaches to research, development, and / or commercialization of products candidates in the territories in which our collaboration partners lead research, development, and / or commercialization; • collaborators might not pursue research, development, and / or commercialization of collaboration drug candidates or might elect not to continue or renew research, development, and / or commercialization programs based on nonclinical and / or clinical trial results, changes in their strategic focus due to the acquisition of competing products, availability of funding, or other factors, such as a business combination that diverts resources or creates competing priorities; • collaborators might delay, provide insufficient resources to, or modify or stop research or clinical development for collaboration drug candidates or require a new formulation of a drug candidate for clinical testing; • collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our drug candidates or require a new formulation of a drug candidate for nonclinical and / or clinical testing; • collaborators with sales, marketing, and distribution rights to one or more drug candidates might not commit sufficient resources to sales, marketing, and distribution or might otherwise fail to successfully commercialize those drug candidates; • collaborators might not properly maintain or defend our intellectual property rights or might use our intellectual property improperly or in a way that jeopardizes our intellectual property or exposes us to potential liability; • collaboration activities might result in the collaborator having intellectual property covering our activities or drug candidates,

which could limit our rights or ability to research, develop, and / or commercialize our drug candidates; • collaborators might not be in compliance with laws applicable to their activities under the collaboration, which could impact the collaboration or us; • disputes might arise between us and a collaborator that could cause a delay or termination of the collaboration or result in costly litigation that diverts management attention and resources; and • collaborations might be terminated, which could result in a need for additional capital to pursue further research, development, and / or commercialization of our drug candidates. In addition, funding provided by a collaborator might not be sufficient to advance drug candidates under the collaboration. If a collaborator terminates a collaboration or a program under a collaboration, including by failing to exercise a license or other option under the collaboration, whether because we fail to meet a milestone or otherwise, any potential revenue from the collaboration would be significantly reduced or eliminated. In addition, we will likely need to either secure other funding to advance research, development, and / or commercialization of the relevant drug candidate or abandon that program, the development of the relevant drug candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development, and / or commercialization of the relevant drug candidates. Any one or more of these risks, if realized, could reduce or eliminate future revenue from drug candidates under our collaborations, and could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects. If clinical trials of our drug candidates are prolonged, delayed, suspended, or terminated, we may be unable to commercialize our drug candidates on a timely basis, if at all, which would require us to incur additional costs and delay or prevent our receipt of any revenue from potential product sales. We cannot predict whether we will encounter problems with the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for NNC6019, the Phase 1 clinical trial for ~~PRX005~~ **BMS- 986446** , the Phase 1 clinical ~~trial~~ **trials** for PRX012, or any other future clinical trials that will cause us or any regulatory authority to delay, suspend or terminate those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing or planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular drug candidate: • conditions imposed on us by the FDA, the EMA, or other comparable regulatory authorities regarding the scope or design of our clinical trials; • delays in obtaining, or our inability to obtain, required approvals from institutional review boards (“ IRBs ”) or other reviewing entities at clinical sites selected for participation in our clinical trials; • insufficient supply or deficient quality of our drug candidates or other materials necessary to conduct our clinical trials; • delays in obtaining regulatory authority authorization for the conduct of our clinical trials; • lower than anticipated enrollment and / or retention rate of subjects in our clinical trials, which can be impacted by a number of factors, including size of patient population, design of trial protocol, trial length, eligibility criteria, perceived risks and benefits of the drug candidate, patient proximity to trial sites, patient referral practices of physicians, availability of other treatments for the relevant disease, and competition from other clinical trials; • slower than expected rates of events in trials with a ~~composite~~ primary endpoint that is event- based; • serious and unexpected drug- related side effects experienced by subjects in clinical trials; or • failure of our third- party contractors and collaborators to meet their contractual obligations to us or otherwise meet their development or other objectives in a timely manner. Further, conducting clinical trials in foreign countries, as we do and may continue do for our drug candidates, presents potential additional risks for our clinical trials. These risks include the failure in foreign countries to adhere to clinical protocol as a result of differences in regional or local healthcare services or customs, obtaining clinical data and / or clinical samples from sites in such foreign countries, managing additional administrative burdens associated with foreign regulatory requirements, as well as political and economic risks relevant to such foreign countries. We are dependent upon Roche with respect to further development of prasinezumab. Under the terms of our collaboration with Roche, Roche is responsible for that further development, including the conduct of the ongoing Phase 2 and Phase 2b clinical trials and any future clinical trial of that drug candidate. We are dependent upon Novo Nordisk with respect to further development of NNC6019, including the Phase 2 clinical trial and any future clinical trial of that drug candidate. **We are dependent upon BMS with respect to further development of BMS- 986446, including the Phase 1 clinical trial and any future clinical trial of that drug candidate.** Clinical trials may also be delayed or terminated as a result of ambiguous or negative data or results. In addition, a clinical trial may be delayed, suspended or terminated by us, the FDA, the EMA or other comparable regulatory authorities, the IRBs ~~at~~ **for** the sites where the IRBs are overseeing a trial, or the safety oversight committee overseeing the clinical trial at issue due to a number of factors, including: • failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols; • inspection of the clinical trial operations or trial sites by the FDA, the EMA, or other regulatory authorities resulting in the imposition of a clinical hold on or imposition of additional conditions for the conduct of the trial; • interpretation of data by the FDA, the EMA, or other regulatory authorities; • requirement by the FDA, the EMA, or other regulatory authorities to perform additional studies; • failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy or adequate safety; • unforeseen safety issues; or • lack of adequate funding to continue the clinical trial. Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to regulatory authorities and IRBs for reexamination, which may impact the cost, timing, or successful completion of a clinical trial **. For example, the FDA may modify or enhance clinical trial requirements which could affect enrollment and retention of patients. Such effects on recruitment and retention of patients may hinder or delay a clinical trial, which could increase costs and delay clinical programs** . We do not know whether our clinical trials will be conducted as planned, will need to be restructured, or will be completed on schedule, if at all. Delays in our clinical trials will result in increased development costs for our drug candidates. In addition, if we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for our drug candidates may be delayed or harmed and our ability to generate product revenues will be delayed or jeopardized. Furthermore, 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 regulatory approval of a drug candidate. The regulatory approval processes of the FDA, the

EMA, and other comparable regulatory authorities are lengthy, time consuming, and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed. The time required to obtain approval by the FDA, the EMA, and other comparable regulatory authorities is inherently unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate' s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any drug candidate, and it is possible that none of our existing drug candidates or any drug candidates we may seek to develop in the future will ever obtain regulatory approval. Our drug candidates could fail to receive regulatory approval for many reasons, including the following: • the FDA, the EMA, or comparable regulatory authorities may disagree with the design, implementation, or conduct of our clinical trials; • we may be unable to demonstrate to the satisfaction of the FDA, the EMA, or comparable regulatory authorities that a drug candidate is safe and effective for its proposed indication; • the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA, or comparable regulatory authorities for approval; • we may be unable to demonstrate that a drug candidate' s clinical and other benefits outweigh its safety risks; • the FDA, the EMA, or comparable regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials; • the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of ~~a~~ an NDA or a BLA to the FDA, a Marketing Authorization Application (" MAA ") to the EMA, or similar applications to comparable regulatory authorities; • the FDA, the EMA, or comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; or • the approval policies or regulations of the FDA, the EMA, or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations, and / or growth prospects ~~. Separately, in response to the COVID- 19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on- site inspections of domestic manufacturing facilities subject to a risk- based prioritization system. In May 2021, the FDA updated its guidance, first published in August 2020, clarifying how it intends to conduct inspections during the COVID- 19 pandemic, including how it plans to determine which inspections are " mission critical. " The FDA intends to use this risk- based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID- 19 pandemic, including providing guidance regarding the conduct of clinical trials. If global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, or impact reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business~~ . In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates. The FDA or other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction. We are and may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the United States population and United States medical practice; (2) the trials are performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on- site inspection by the FDA, or if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any other comparable foreign regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any other comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time- consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval for commercialization in the applicable jurisdiction. Even if our drug candidates receive regulatory approval in one country or jurisdiction, we may never receive approval or commercialize our products in other countries or jurisdictions. In order to market drug candidates in a particular country or jurisdiction, we must establish and comply with numerous and varying regulatory requirements of that country or jurisdiction, including with respect to safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain, for example, FDA approval in the U. S. or EMA approval in the EU. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U. S. and EMA approval in the EU as well as other risks. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another country or jurisdiction, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in one country or jurisdiction or any delay or setback in obtaining such approval would impair our

ability to develop other markets for that drug candidate. Although we have obtained agreement with the FDA on a special protocol assessment (“ SPA ”) with regard to our Phase 3 AFFIRM- AL **clinical** trial of birtamimab, ~~an~~ **a** SPA does not guarantee approval of birtamimab or any other particular outcome from regulatory review. On January 27, 2021, the FDA agreed to ~~an~~ **a** SPA for our Phase 3 AFFIRM- AL clinical trial of birtamimab. The FDA’ s SPA process is designed to facilitate the FDA’ s review and approval of drugs by allowing the FDA to evaluate proposed critical design features of certain clinical trials that are intended to form the primary basis for determining a drug candidate’ s efficacy and safety. Upon specific request by a clinical trial sponsor, the FDA will evaluate the study protocol and statistical analysis plan and respond to a sponsor’ s questions regarding protocol design and scientific and regulatory requirements. FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design for the trial, such as entry criteria, endpoints, size, duration, and planned analyses, are acceptable to support an application for regulatory approval of the drug candidate with respect to the effectiveness of and safety for the indication studied. All agreements and disagreements between the FDA and the sponsor regarding a SPA must be clearly documented in ~~an~~ **a** SPA letter or the minutes of a meeting between the sponsor and the FDA. Although the FDA has agreed to the SPA for our Phase 3 AFFIRM- AL clinical trial with respect to the primary endpoint and certain other aspects of the clinical trial, a SPA agreement does not guarantee approval of a drug candidate. The FDA may limit the scope of its agreement to ~~an~~ **a** SPA agreement to certain, specific aspects of the clinical trial design. Even if the FDA agrees to the design, execution, and analysis proposed in a protocol reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, a SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor fails to comply with the agreed upon study protocol, or the relevant data, assumptions, or information provided by the sponsor in a request for the SPA change or are found to be false or to omit relevant facts. In addition, even after a SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to the modification of the study protocol and / or statistical analysis plan. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than the sponsor, the FDA may not deem the data sufficient to support an application for regulatory approval. Both before and after marketing approval, our drug candidates are subject to ongoing regulatory requirements and continued regulatory review, and if we fail to comply with these continuing requirements, we could be subject to a variety of sanctions and the sale of any approved products could be suspended. Both before and after regulatory approval to market a particular drug candidate, adverse event reporting, manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record keeping, and reporting related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, as well as continued compliance with current good manufacturing practice (“ cGMP ”) requirements and current good clinical practice (“ cGCP ”) requirements for any clinical trials that we conduct. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or not previously observed in clinical trials, or problems with our third- party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA, the EMA, or other comparable regulatory authorities could subject us to administrative or judicially imposed sanctions, including: • restrictions on the marketing of our products or their manufacturing processes; • warning letters; • civil or criminal penalties; • fines; • injunctions; • product seizures or detentions; • import or export bans; • voluntary or mandatory product recalls and related publicity requirements; • suspension or withdrawal of regulatory approvals; • total or partial suspension of production; and • refusal to approve pending applications for marketing approval of new products or supplements to approved applications. The policies of the FDA, the EMA, or other comparable regulatory authority may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. 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, which would adversely affect our business, prospects and ability to achieve or sustain profitability. If side effects are identified during the time our drug candidates are in development, or, if they are approved by applicable regulatory authorities, after they are on the market, we may choose to or be required to perform lengthy additional clinical trials, discontinue development of the affected drug candidate, change the labeling of any such products, or withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues. Undesirable side effects caused by our drug candidates could 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 regulatory approval by the FDA, the EMA, or other comparable regulatory authorities. Drug- related side effects could affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Even if any of our drug candidates receives marketing approval, as greater numbers of patients use a drug following its approval, an increase in the incidence or severity of side effects or the incidence of other post- approval problems that were not seen or anticipated during pre- approval clinical trials could result in a number of potentially significant negative consequences, including: • regulatory authorities may withdraw their approval of the product; • regulatory authorities may require the addition of labeling statements, such as contraindications, warnings, or precautions; or impose additional safety monitoring or reporting requirements; • we may be required to change the way the product is administered, or to conduct

additional clinical trials; • we could be sued and held liable for harm caused to patients; and • our reputation may suffer. Any of these events could substantially increase the costs and expenses of developing, commercializing and marketing any such drug candidates or could harm or prevent sales of any approved products. We deal with hazardous materials and must comply with environmental laws and regulations which can be expensive and restrict how we do business. Some of our research and development activities involve the controlled storage, use, and disposal of hazardous materials. We are subject to U. S. federal, state, local, and other countries' and jurisdictions' laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials, and we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Because we believe that our laboratory and materials handling policies and practices sufficiently mitigate the likelihood of materials liability or third- party claims, we currently carry no insurance covering such claims. An accident could damage, or force us to shut down, our operations. Risks Related to the Commercialization of Our Drug Candidates Even if any of our drug candidates receives regulatory approval, if such approved product does not achieve broad market acceptance, the revenues that we generate from sales of the product will be limited. Even if any drug candidates we may develop or acquire in the future obtain regulatory approval, they may not gain broad market acceptance among physicians, healthcare payers, patients and the medical community. The degree of market acceptance for any approved drug candidate will depend on a number of factors, including: • the indication and label for the product and the timing of introduction of competitive products; • demonstration of clinical safety and efficacy compared to other products; • prevalence, frequency, and severity of adverse side effects; • availability of coverage and adequate reimbursement from managed care plans and other third- party payers; • convenience and ease of administration; • cost- effectiveness; • other potential advantages of alternative treatment methods; and • the effectiveness of marketing and distribution support of the product. Consequently, even if we discover, develop, and commercialize a product, the product may fail to achieve broad market acceptance and we may not be able to generate significant revenue from the product. The success of prasinezumab in the United States, if approved, will be dependent upon the strength and performance of our collaboration with Roche. If we fail to maintain our existing collaboration with Roche, such termination would likely have a material adverse effect on our ability to develop and commercialize prasinezumab and our business. Furthermore, in May 2021, we opted out of profit and loss sharing with Roche for prasinezumab in Parkinson' s disease; however if we opt out of profit and loss sharing for any other Licensed Products and / or indications, our revenues from such other Licensed Products and / or indications will be reduced. The success of sales of prasinezumab in the U. S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize prasinezumab, if approved by the FDA, pursuant to the License Agreement we entered into in December 2013. Our collaboration with Roche is complex, particularly with respect to future U. S. commercialization of prasinezumab, with respect to financial provisions, allocations of responsibilities, cost estimates, and the respective rights of the parties in decision making. Accordingly, significant aspects of the development and commercialization of prasinezumab require Roche to execute its responsibilities under the arrangement, or require Roche' s agreement or approval, prior to implementation, which could cause significant delays that may materially impact the potential success of prasinezumab in the U. S. In addition, Roche may under some circumstances independently develop products that compete with prasinezumab, or Roche may decide to not commit sufficient resources to the development, commercialization, marketing and distribution of prasinezumab. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize prasinezumab, our business could be materially adversely affected. Furthermore, the terms of the License Agreement provide that Roche has the ability to terminate such arrangement for any reason after the first anniversary of the License Agreement at any time upon 90 days' notice (if prior to first commercial sale) or 180 days' notice (if after first commercial sale). For example, even if prasinezumab was approved by the FDA, Roche may determine that the outcomes of clinical trials made prasinezumab a less attractive commercial product and terminate our collaboration. If the License Agreement is terminated, our business and our ability to generate revenue from sales of prasinezumab could be substantially harmed as we will be required to develop, commercialize, and build our own sales and marketing organization, or enter into another strategic collaboration in order to develop and commercialize prasinezumab in the U. S. Such efforts may not be successful and, even if successful, would require substantial time and resources to carry out. The manner in which Roche launches prasinezumab, if approved by the FDA, including the timing of launch and potential pricing, will have a significant impact on the ultimate success of prasinezumab in the U. S., and the success of the overall commercial arrangement with Roche. If launch of commercial sales of prasinezumab in the U. S. by Roche is delayed or prevented, our revenue will suffer and our stock price may decline. Further, if launch and resulting sales by Roche are not deemed successful, our business would be harmed and our stock price may decline. Any lesser effort by Roche in its prasinezumab sales and marketing efforts may result in lower revenue and thus lower profits with respect to the U. S. The outcome of Roche' s commercialization efforts in the U. S. could also have a negative effect on investors' perception of potential sales of prasinezumab outside of the U. S., which could also cause a decline in our stock price. In May 2021, we opted out of profit and loss sharing with Roche for prasinezumab in Parkinson' s disease. However, pursuant to the License Agreement, we are responsible for 30 % of all development and commercialization costs for any future Licensed Products and / or indications (other than Parkinson' s disease with prasinezumab) that we opt to co- develop, in each case unless we elect to opt out of profit and loss sharing. If we elect to opt out of profit and loss sharing, we will instead receive sales milestones and royalties, and our revenue, if any, from such other Licensed Products and / or indications will be reduced. Our right to co- develop Licensed Products and / or indications under the License Agreement (other than Parkinson' s disease with prasinezumab for which we have opted out of co- development) will terminate if we commence certain studies for a competitive product that treats Parkinson' s disease or other indications that we opted to co- develop. In addition, our right to co- promote prasinezumab and

other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson' s disease. Moreover, under the terms of the License Agreement, we rely on Roche to provide us estimates of their costs, revenue, and revenue adjustments and royalties, which estimates we use in preparing our quarterly and annual financial reports. If the underlying assumptions on which Roche' s estimates were based prove to be incorrect, actual results or revised estimates supplied by Roche that are materially different from the original estimates could require us to adjust the estimates included in our reported financial results. If material, these adjustments could require us to restate previously reported financial results, which could have a negative effect on our stock price. Our ability to receive any significant revenue from prasinezumab will be dependent on Roche' s efforts and may result in lower levels of income than if we marketed or developed our drug candidates entirely on our own. Roche may not fulfill its obligations or carry out marketing activities for prasinezumab as diligently as we would like. We could also become involved in disputes with Roche, which could lead to delays in or termination of development or commercialization activities and time- consuming and expensive litigation or arbitration. If Roche terminates or breaches the License Agreement, or otherwise decides not to complete its obligations in a timely manner, the chances of successfully developing, commercializing, or marketing prasinezumab would be materially and adversely affected. Outside of the United States, we are solely dependent on the efforts and commitments of Roche, either directly or through third parties, to further develop and, if prasinezumab is approved by applicable regulatory authorities, commercialize prasinezumab. If Roche' s efforts are unsuccessful, our ability to generate future product sales from prasinezumab outside the United States would be significantly reduced. Under our License Agreement, outside of the U. S., Roche has responsibility for developing and commercializing prasinezumab and any future Licensed Products targeting α- synuclein. As a consequence, any progress and commercial success outside of the U. S. is dependent solely on Roche' s efforts and commitment to the program. For example, Roche may delay, reduce, or terminate development efforts relating to prasinezumab outside of the U. S., or under some circumstances independently develop products that compete with prasinezumab, or decide not to commit sufficient resources to the commercialization, marketing, and distribution of prasinezumab. In the event that Roche does not diligently develop and commercialize prasinezumab, the License Agreement provides us the right to terminate the License Agreement in connection with a material breach uncured for 90 days after notice thereof. However, our ability to enforce the provisions of the License Agreement so as to obtain meaningful recourse within a reasonable timeframe is uncertain. Further, any decision to pursue available remedies including termination would impact the potential success of prasinezumab, including inside the U. S., and we may choose not to terminate as we may not be able to find another partner and any new collaboration likely will not provide comparable financial terms to those in our arrangement with Roche. In the event of our termination, this may require us to develop and commercialize prasinezumab on our own, which is likely to result in significant additional expense and delay. Significant changes in Roche' s business strategy, resource commitment and the willingness or ability of Roche to complete its obligations under our arrangement could materially affect the potential success of the drug candidate. Furthermore, if Roche does not successfully develop and commercialize prasinezumab outside of the U. S., our potential to generate future revenue outside of the U. S. would be significantly reduced. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell approved products, we may be unable to generate product revenue. We do not currently have a fully- scaled organization for the sales, marketing, and distribution of pharmaceutical products. In order to market any products that may be approved by the FDA, the EMA, or other comparable regulatory authorities, we must build our sales, marketing, managerial, and other non- technical capabilities or make arrangements with third parties to perform these services. We have entered into the License Agreement with Roche for the development of prasinezumab and may develop our own sales force and marketing infrastructure to co- promote prasinezumab in the U. S. for the treatment of Parkinson' s disease and any future Licensed Products approved for Parkinson' s disease in the U. S. If we exercise our co- promotion option and are unable to develop our own sales force and marketing infrastructure to effectively commercialize prasinezumab or other Licensed Products, our ability to generate additional revenue from potential sales of prasinezumab or such products in the U. S. may be harmed. In addition, our right to co- promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson' s disease. For any other products that may be approved, if we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable. If government and third- party payers fail to provide coverage and adequate reimbursement rates for any of our drug candidates that receive regulatory approval, our revenue and prospects for profitability will be harmed. In both U. S. and non- U. S. markets, our sales of any future products will depend in part upon the availability of reimbursement from third- party payers. Such third- party payers include government health programs such as Medicare **and Medicaid** , managed care providers, private health insurers, and other organizations. There is significant uncertainty related to the third- party coverage and reimbursement of newly approved drugs. Coverage and reimbursement may not be available for any drug that we or our collaborators commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Third- party payers often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Third- party payers are also increasingly attempting to contain healthcare costs by demanding price discounts or rebates limiting both coverage and the amounts that they will pay for new drugs, and, as a result, they may not cover or provide adequate payment for our drug candidates. We might need to conduct post- marketing studies in order to demonstrate the cost- effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost- effective. Adequate third- party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any drug candidates for which marketing approval is obtained. **Additionally, pursuant to the Medicaid Drug Rebate Statute, we will be required to participate in the Medicaid Drug Rebate Program in order for federal payment to**

be available for our products under Medicaid and Medicare Part B. Under the Medicaid Drug Rebate Program, we will be required to, among other things, pay a rebate to each state Medicaid program for quantities of our products utilized on an outpatient basis (with some exceptions) that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. Medicaid Drug Rebate Program rebates are calculated using a statutory formula, state- reported utilization data, and pricing data that are calculated and reported by us on a monthly and quarterly basis to the Centers for Medicare and Medicaid Services (" CMS "). These data include the average manufacturer price and, in the case of single source and innovator multiple source products, the best price for each drug. The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, and negatively impact our ability to generate revenue from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval. U. S. and other governments continue to propose and pass legislation designed to reduce the cost of healthcare. In the U. S., we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the U. S. will continue to put pressure on pharmaceutical product pricing. For example, in 2010, the U. S. Patient Protection and Affordable Care Act, as amended by the U. S. Health Care and Education Reconciliation Act (collectively, the " ACA "), was enacted. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the ACA of importance to the pharmaceutical industry are the following: • an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs; • an increase in the minimum rebates a manufacturer must pay under the U. S. Medicaid Drug Rebate Program to 23. 1 % and 13. 0 % of the average manufacturer price for branded and generic drugs, respectively; • expansion of healthcare fraud and abuse laws, including the U. S. False Claims Act **(" FCA ")** and the U. S. Anti- Kickback Statute, new government investigative powers and enhanced penalties for non- compliance ~~; • a new Medicare Part D coverage gap discount program, under which manufacturers must now agree to offer 70 percent point- of- sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer' s outpatient drugs to be covered under Medicare Part D~~ ; • extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; • expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133 % of the federal poverty level, thereby potentially increasing a manufacturer' s Medicaid rebate liability; • a licensure framework for follow- on biologic products; • expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; • **implementation of** ~~new requirements under~~ the federal ~~Open~~ **Physician** Payments ~~program~~ **Sunshine Act, which requires pharmaceutical manufacturers, among others, to annually track** and ~~its implementing regulations~~ **report all payments and other transfers of value they make to certain healthcare providers, as well as physician ownership held in the company** ; • a ~~new~~ requirement **for manufacturers and distributors** to annually report drug samples that **they** ~~manufacturers and distributors~~ provide to physicians; and • ~~a new~~ **establishment of the** Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. 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, which went into effect in 2013 and will stay in effect through **the first six months of the FY** ~~2030~~ **2032 sequestration order** ~~, with the exception of a temporary suspension from May 1, 2020, through March 31, 2021~~ , unless additional congressional action is taken **, with the exception of a temporary suspension from May 1, 2020, through March 31, 2022, and a subsequent 1 % cut in Medicare payments in effect from March 31, 2022 to July 1, 2022, due to the COVID- 19 pandemic** . In 2013, the U. S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations. Since its enactment, there have been judicial, executive, and Congressional challenges to certain aspects of the ACA. ~~The~~ **While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law, including the repeal, effective January 1, 2019, of the tax- based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the " individual mandate. " On June 17, 2021, the** U. S. Supreme Court ~~is currently reviewing~~ **dismissed the most recent judicial challenge to the ACA brought by several states who argued that, without the individual mandate, the entire ACA was unconstitutional. The Supreme Court' s dismissal of the lawsuit did not specifically rule on** the constitutionality of the ACA **. Moreover** ~~in its entirety~~ , ~~although it~~ **President Biden signed into law the Inflation Reduction Act (IRA) on August 16, 2022, which allows Medicare to: beginning in 2026, establish a " maximum fair price " for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with CMS; and, beginning in 2023, penalize drug companies that raise prices for products covered under Medicare Parts**

B and D faster than inflation, among other reforms. CMS has recently taken steps to implement the IRA, including: on June 30, 2023, issuing guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the " maximum fair price " provision that would become effective in 2026; on August 29, 2023, releasing the initial list of ten drugs subject to price negotiations; on November 17, 2023, releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in a phase- in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; and on December 14, 2023, releasing a list of 48 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2024 to March 31, 2024. It is unclear how **future regulatory actions to implement** the ~~Supreme Court~~ **IRA, as** ~~will~~ **well** ~~rule~~ **as the outcome of pending litigation against the IRA brought against the Department of Health and Human Services (HHS), the Secretary of HHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA' s drug price negotiation provisions, may affect our products and future profitability** . ~~It is also unclear how~~ **Additionally, on October 14, 2022, President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of HHS to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. On February 14, 2023, HHS issued a report in response to the October 14, 2022 Executive Order, which, among** other ~~efforts~~ **things** , ~~if any,~~ **selects three potential drug affordability and accessibility models** to ~~challenge~~ **be tested by the CMS Innovation Center. Specifically** , ~~repeal,~~ **the report addresses: (1) a model that would allow Part D Sponsors to establish a " high- value drug list " setting the maximum co- payment amount** ~~or~~ **for** ~~replace the ACA will impact the law~~ **certain common generic drugs at $ 2** . ~~The ultimate content~~ **00; (2) a Medicaid- focused model that would establish a partnership between CMS** , ~~timing~~ **manufacturers** , **and state Medicaid agencies that would result in multi- state outcomes- based agreements or certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts** ~~or~~ **for Accelerated Approval Program drugs to advance** ~~effect of any healthcare reform legislation on~~ the **developments of novel treatments** ~~U. S. healthcare industry is unclear~~ . We expect that 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. Legislation and regulations affecting the pricing of pharmaceuticals might change before our drug candidates are approved for marketing. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs. There can be no assurance that our drug candidates, if they are approved for sale in the U. S. or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost- effective by third- party payers, that coverage or an adequate level of reimbursement will be available, or that third- party payers' reimbursement policies will not adversely affect our ability to sell our drug candidates profitably if they are approved for sale. The markets for our drug candidates are subject to intense competition. If we are unable to compete effectively, our drug candidates may be rendered noncompetitive or obsolete. The research, development, and commercialization of new drugs is highly competitive. We will face competition with respect to all drug candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its indication, label, efficacy, safety profile, drug interactions, method of administration, pricing, coverage, reimbursement, and level of promotional activity relative to those of competing drugs. Furthermore, many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and other public and private research organizations are pursuing the development of novel drugs that target the same indications we are targeting with our research and development program. We face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available. Many of our competitors have: • significantly greater financial, technical and human resources than we have and may be better equipped to discover, develop, manufacture, and commercialize drug candidates; • more extensive experience in nonclinical testing and clinical trials, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products; • drug candidates that have been approved or are in late- stage clinical development; and / or • collaborative arrangements in our target markets with leading companies and research institutions. Competitive products may render our research and development program obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and / or the widespread adoption or increased utilization of any vaccine or development of other products or treatments for the diseases we are targeting could render any of our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for a drug candidate, we will face competition based on the safety and effectiveness of the approved product, the timing of its entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, coverage, reimbursement, price, patent position and other factors. Even if we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful. Our drug candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated. Our current drug candidates are regulated by the FDA as biologic products and we intend to seek approval for these products pursuant to the BLA pathway. The U. S. Biologics Price Competition and Innovation Act of 2009 (the " BPCIA ") created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as " interchangeable " based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA, and cannot be approved by the

FDA until 12 years after the original branded product was approved under a BLA. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. However, during the 12- year period of reference product exclusivity, another company may obtain FDA licensure and market a competing version of the reference product if the FDA approves a full de novo BLA, not an abbreviated BLA for a biosimilar product, for the competing product containing that applicant' s own preclinical data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity and potency of its product. The law is complex and is still being interpreted and implemented by the FDA. Any processes adopted by the FDA to implement the BPCIA could have a material adverse effect on the future commercial prospects for our biologic products. In addition, there has been discussion of whether Congress should reduce the 12- year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate implementation of the BPCIA is subject to significant uncertainty. We believe that any of our drug candidates approved as a biologic product under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our drug candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non- biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. We may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for supplemental market exclusivity. Birtamimab has been granted Orphan Drug Designation by both the FDA and EMA for the treatment of AL amyloidosis. In addition, we may seek Orphan Drug Designation for one or more of our current or future drug candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drug products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200, 000 in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user- fee waivers. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and licensure process. If a drug product that has Orphan Drug Designation subsequently receives the first FDA approval or licensure for a particular active ingredient for the disease for which it has such designation, the drug product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the biological product was designated. As a result, even if one of our drug candidates receives orphan exclusivity, the FDA can still approve or license other drug products that have a different active ingredient for use in treating the same indication or disease. Further, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our drug product. A Fast Track designation by the FDA, even if granted for current or future drug candidates, may not lead to a faster development or regulatory review, licensure process and does not increase the likelihood that our drug candidates will receive marketing licensure. Birtamimab and PRX012 have been granted Fast Track Designation by the FDA for the treatment of AL amyloidosis and Alzheimer' s disease, respectively. In addition, we may seek Fast Track designation for one or more of our future drug candidates. If a drug candidate is intended for the treatment of a serious condition and demonstrates the potential to address an unmet medical need for this condition, the sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for our drug candidates, but there is no assurance that the FDA will grant this status to any of our drug candidates. The FDA has broad discretion whether or not to grant Fast Track designation, and even if we consider a particular drug candidate to be eligible for this designation, there is no assurance that it will be granted by the FDA. Even if we do receive Fast Track designation, we may not experience a faster review or approval compared to other, non- expedited FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our applicable clinical development program. Marketing applications filed by sponsors of products granted Fast Track designation may qualify for priority review under FDA policies and procedures, but Fast Track designation does not assure any such review or ultimate marketing approval by the FDA. We are subject to healthcare and other laws and regulations, including anti- bribery, anti- kickback, fraud and abuse, false claims, and physician payment transparency laws and regulations, which could expose us to criminal, civil and / or administrative sanctions and penalties; exclusion from governmental healthcare programs or reimbursements; contractual damages; and reputational harm. Our operations and activities are directly, or indirectly through our service providers and collaborators, subject to numerous healthcare and other laws and regulations, including, without limitation, those relating to anti- bribery, anti- kickback, fraud and abuse, false claims, physician payment transparency, and health information privacy and security, in the U. S., the EU, and other countries and jurisdictions in which we conduct our business. These laws include: • the U. S. **federal** Anti- Kickback Statute, **an intent- based federal criminal statute** which prohibits, among other things, persons **and entities** from knowingly and willfully soliciting, receiving, offering **, providing,** or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase **, lease, order or arrangement for,** or recommendation of an item or service ~~reimbursable under~~ **for which payment may be made, in whole or in part, by** a federal healthcare program, such as the Medicare and Medicaid programs. 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 **. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if any " one purpose " of an arrangement involving remuneration is to induce referrals of federal**

healthcare program business, the federal Anti- Kickback Statute has been violated. The federal Anti- Kickback Statute applies to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other hand, including, for example, consulting / speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. Although there are several statutory exceptions and regulatory safe harbors to the federal Anti- Kickback Statute that protect certain common industry activities from prosecution, these exceptions and safe harbors are narrowly drawn. Arrangements that do not fully satisfy all elements of an available exception or safe harbor are evaluated based on the specific facts and circumstances and are typically subject to increased scrutiny ; • U. S. federal false claims laws, including the **civil FCA** ~~False Claims Act~~ , which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, claims for payment **or approval** from Medicare, Medicaid, or other third- party payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the **ACA specified** ~~government may assert~~ that ~~a~~ **any** ~~claim~~ **claims submitted as a** ~~including items and services resulting~~ **result** ~~from~~ **of** a violation of the ~~U. S.~~ federal Anti- Kickback Statute ~~constitutes~~ **constitute** ~~a~~ false ~~or fraudulent claim~~ **claims** ~~for purposes of~~ **and are subject to enforcement under** the **federal** False Claims Act **. Violations of the FCA may be subject to significant civil fines and penalties for each false claim, currently ranging from $ 13, 946- $ 27, 894 per false claim, treble damages, and potential exclusion from participation in federal healthcare programs** ; • HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U. S. federal 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; • the U. S. **federal** Physician ~~Payment~~ **Payments** Sunshine Act, which requires ~~applicable~~ **certain** manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program, **among others** ~~with specific exceptions~~ , to **track and** report annually to ~~the Centers for Medicare & Medicaid Services (~~ CMS ~~)~~ information related to " payments or other transfers of value " made to **U. S.- licensed** physicians (defined to include doctors, dentists, optometrists, podiatrists and **licensed** chiropractors) **, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiology assistants, certified nurse midwives,** and teaching hospitals **; as well as tracking** and ~~applicable manufacturers and applicable group purchasing organizations to report~~ **reporting of** ~~annually to CMS~~ ownership and investment interests held by the **U. S.- licensed** physicians (as defined by statute) and their immediate family members ~~. Effective January 1, 2022, these reporting obligations extended to include transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse midwives~~ ; • **analogous** state laws and regulations that **may** apply to sales or marketing arrangements ~~; apply to~~ **and claims for** healthcare items or services reimbursed by non- governmental third- party payers, including private insurers **, that may be broader in scope than their federal equivalents** ; **state laws and regulations that** require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines ~~; that~~ **and the relevant compliance guidance promulgated by the federal government or otherwise** restrict payments that may be made to healthcare providers; **state laws and regulations that** require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or **require the disclosure of** marketing expenditures **and other pricing information** ; and • similar and other laws and regulations in the U. S. (federal, state and local), in the EU (including member countries), and other countries and jurisdictions ~~. On September 4, 2018, we received a subpoena from the U. S. Department of Justice requesting the production of documents relating to our NEOD001 development program. We completed the production of documents in July 2019. Since that time, the Department of Justice has not requested that we provide any additional information. We cannot predict the outcome of this matter or whether any government agency will take further action. If further action is taken, it could divert the attention of management and require the devotion of a substantial amount of time and resources~~ . Ensuring our compliance with applicable laws and regulations involves substantial costs, and it is possible that governmental authorities or third parties will assert that our business practices fail to comply with these laws and regulations. If our actions are found to be in violation of any laws and regulations, we may be subject to significant civil, criminal, and administrative damages, penalties, and fines, as well as exclusion from participation in government healthcare programs, curtailment or restructuring of our operations, and reputational harm, any of which could have a material adverse effect on our business, financial condition, or results of operations. If a successful product liability or clinical trial claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, we could incur substantial liability. The use of our drug candidates in clinical trials and the sale of any products for which we obtain marketing approval will expose us to the risk of product liability and clinical trial liability claims. Product liability claims might be brought against us by consumers, healthcare providers, or others selling or otherwise coming into contact with our products. Clinical trial liability claims may be filed against us for damages suffered by clinical trial subjects or their families. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in: • decreased demand for any approved drug candidates; • impairment of our business reputation; • withdrawal of clinical trial participants; • costs of related litigation; • distraction of management' s attention; • substantial monetary awards to patients or other claimants; • loss of revenues; and • the inability to successfully commercialize any approved drug candidates. We currently have clinical trial liability insurance coverage for all of our clinical trials. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, 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. If and when we obtain marketing approval for any of our drug candidates, we intend to expand our insurance coverage to include the sale of

commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our ordinary share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business. Risks Related to Our Dependence on Third Parties We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of any such clinical trials. We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties, such as consultants, contract research organizations, medical institutions, and clinical investigators to assist us with these activities. Our reliance on these third parties for clinical development activities results in reduced control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have and will enter into agreements with these third parties, we will be responsible for confirming that our clinical trials are conducted in accordance with their general investigational plans and protocols. Moreover, the FDA, the EMA, and other comparable regulatory authorities require us to comply with regulations and standards, commonly referred to as cGCPs, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If we or any of our third- party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or other comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMPs. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. **Requirements regarding clinical trial data may evolve, and any such changes to data requirements may cause the FDA or comparable foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and to require further studies.** To date, we believe our consultants, contract research organizations, and other third parties with which we are working have **generally** performed ~~well~~ **satisfactorily** ; however, if these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with applicable regulations, we **have been, and** may be **,** required to replace them. Although we believe that there are a number of other third- party contractors we could engage to continue these activities, we may not be able to enter into arrangements with alternative third- party contractors or to do so on commercially reasonable terms, which may result in a delay of our planned clinical trials. Accordingly, we may be delayed in obtaining regulatory approvals for our drug candidates and may be delayed in our efforts to successfully develop our drug candidates. In addition, our third- party contractors are not our employees, and except for remedies available to us under our agreements with such third- party contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. If third- party contractors do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. If we do not establish additional strategic collaborations, we may have to alter our research, development, and / or commercialization plans. Research, development, and potential commercialization of our drug candidates will require substantial additional cash to fund expenses. Our strategy includes potentially collaborating with additional leading pharmaceutical and biotechnology companies to assist us in furthering research, development, and / or potential commercialization of some of our drug candidates in some or all geographies. It may be difficult to enter into one or more of such collaborations in the future. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time- consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all, in which case we may have to curtail the development of a particular drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our drug candidates to market and generate product revenue. We have no manufacturing capacity and depend on third- party manufacturers to supply us with nonclinical and clinical trial supplies of all of our drug candidates, and we will depend on third- party manufacturers to supply us with any drug product for commercial sale if we obtain marketing approval from the FDA, the EMA, or any other comparable regulatory authority for any of our drug candidates. We do not own or operate facilities for the manufacture, packaging, labeling, storage, testing, or distribution of nonclinical or clinical supplies of any of our drug candidates. We instead contract with and rely on third parties to manufacture, package, label, store, test, and distribute nonclinical and clinical supplies of our drug candidates, and we plan to continue to do so for the foreseeable future. We also rely on third- party consultants to assist us with managing these third ~~-~~-parties and with our manufacturing strategy. **Certain** ~~If any~~ of these third ~~-~~-parties **have** ~~fail~~ **failed** to perform these activities for us **and any of these third parties may fail to perform these activities for us in the future** , **which could cause** nonclinical or clinical development of our drug candidates ~~could~~ **to** be delayed, which could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. If the FDA, the EMA, or any other comparable regulatory authority approves any of our drug candidates for commercial sale, we expect to continue to rely, at least initially, on third ~~-~~-parties to manufacture, package, label, store, test, and distribute commercial supplies of such approved drug product. Significant scale- up of manufacturing may require additional

comparability validation studies, which the FDA, the EMA, or other comparable regulatory authorities must review and approve. Our third- party manufacturers might not be able to successfully establish such comparability or increase their manufacturing capacity in a timely or economic manner, or at all. If our third- party manufacturers are unable to successfully establish comparability or increase their manufacturing capacity for any drug product, and we are unable to timely establish our own manufacturing capabilities, the commercial launch of that drug candidate could be delayed or there could be a shortage in supply, which could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. Our third- party manufacturers' facilities could be damaged by fire, power interruption, information system failure, natural disaster or other similar event, which could cause a delay or shortage in supplies of our drug candidates, which could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. Our drug candidates require, and any future drug product will require, precise, high quality manufacturing, packaging, labeling, storage, and testing that meet stringent cGMP, other regulatory requirements and other standards. Our third- party manufacturers are subject to ongoing periodic and unannounced inspections by the FDA, the EMA, and other comparable regulatory authorities to ensure compliance with these cGMPs, other regulatory requirements and other standards. We do not have control over, and are dependent upon, our third- party manufacturers' compliance with these cGMPs, regulations and standards. Any failure by a third- party manufacturer to comply with these cGMPs, regulations or standards or that compromises the safety of any of our drug candidates or any drug product could cause a delay or suspension of production of nonclinical or clinical supplies of our drug candidates or commercial supplies of drug product, cause a delay or suspension of nonclinical or clinical development, product approval and / or commercialization of our drug candidates or drug product, result in seizure or recall of clinical or commercial supplies, result in fines and civil penalties, result in liability for any patient injury or death or otherwise increase our costs, any of which could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. If a third- party manufacturer cannot or fails to perform its contractual commitments, does not have sufficient capacity to meet our nonclinical, clinical or eventual commercial requirements or fails to meet cGMPs, regulations or other standards, we **have been, and** may be **,** required to replace it or qualify an additional third- party manufacturer. Although we believe there are a number of potential alternative manufacturers, the number of manufacturers with the necessary manufacturing and regulatory expertise and facilities to manufacture biologics like our antibodies is limited. In addition, we **have incurred, and** could incur **,** significant additional costs and delays in identifying and qualifying any new third- party manufacturer, due to the technology transfer to such new manufacturer and because the FDA, the EMA, and other comparable regulatory authorities must approve any new manufacturer prior to manufacturing our drug candidates. Such approval would require successful technology transfer, comparability and other testing and compliance inspections. Transferring manufacturing to a new manufacturer could therefore interrupt supply, delay our clinical trials and any commercial launch, and / or increase our costs for our drug candidates, any of which could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. Rentschler Biopharma SE (" Rentschler ") and Catalent **Indiana** ~~Pharma Solutions~~ , LLC (" Catalent **Indiana** ") are our third- party manufacturers of clinical supplies of birtamimab. We are dependent on Rentschler and Catalent **Indiana** to manufacture these clinical supplies. ~~Roche, with whom we are collaborating on development of prasinezumab, manufactured clinical supplies for the Phase 2 and Phase 2b clinical trials for prasinezumab and is expected to do so for any subsequent clinical trials of prasinezumab. We are dependent on Roche to continue to manufacture these clinical supplies. We are dependent on Novo Nordisk, and its third party manufacturers if applicable, to manufacture clinical supplies of NNC6019.~~ Catalent **Pharma Solutions, LLC (" Catalent Pharma ")** and Berkshire Sterile Manufacturing, LLC (" Berkshire ") are our third- party manufacturers of clinical supplies of ~~PRX005~~ **our drug candidate PRX012** . We are dependent on Catalent **Pharma** and Berkshire to manufacture these clinical supplies. ~~Catalent is our third- party manufacturer of clinical supplies of our drug candidate PRX012.~~ We are dependent on ~~Catalent~~ **Roche, and its third- party manufacturers if applicable,** to manufacture ~~these~~ clinical supplies **of prasinezumab. We are dependent on Novo Nordisk, and its third- party manufacturers if applicable, to manufacture clinical supplies of NNC6019. We are dependent on BMS, and its third- party manufacturers if applicable, to manufacture clinical supplies of BMS- 986446** . In July 2021, the Company sold the equity interests of a subsidiary that owns and has exclusive licenses to intellectual property rights and other assets pertaining to the investigational humanized monoclonal antibody known as NNC6019 (formerly PRX004), and we might not realize the anticipated benefits of such transaction. On July 8, 2021, the Company, together with its wholly owned subsidiary, Prothena Biosciences Limited (" PBL "), entered into a Share Purchase Agreement with Novo Nordisk and NNRE (together with Novo Nordisk, " Buyer "), pursuant to which PBL sold and transferred to NNRE, all issued and outstanding ordinary shares of Neotope Neuroscience Limited, a wholly owned subsidiary of PBL, for an aggregate purchase price of up to $ 1. 23 billion. The aggregate purchase price consists of an upfront payment of $ 60 million in cash, subject to customary purchase price adjustments, and an aggregate of $ 1. 17 billion in cash, payable on Buyer' s achievement of certain development, commercialization and net sales- based milestones. On November 21, 2022, we earned a $ 40 million milestone payment. There can be no assurance that such remaining milestones will be met. If we do not receive additional milestone payments as a result of the transaction in anticipated amounts or at all, we may need to seek additional sources of capital to pursue further research, development, and / or commercialization of our drug candidates, and this could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects. We depend on third- party suppliers for key raw materials used in our manufacturing processes, and the loss of these third- party suppliers or their inability to supply us with adequate raw materials could harm our business. We rely on third- party suppliers for the raw materials required for the production of our drug candidates. Our dependence on these third- party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality, and delivery schedules. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our products until a new

source of supply, if any, could be identified and qualified. Although we believe there are currently several other suppliers of these raw materials, we may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our drug candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business. Risks Related to Our Intellectual Property If we are unable to adequately protect or enforce the intellectual property relating to our drug candidates our ability to successfully commercialize our drug candidates will be harmed. Our success depends in part on our ability to obtain patent protection both in the U. S. and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal, factual and scientific questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. Additionally, our ability to obtain patent protection for our drug candidates also depends on our collaborators, partners, contractors, and employees involved in the generation of intellectual property to carry out their contractual duties, including those to assign or license relevant intellectual property rights developed on our behalf to us. In addition, the strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal, factual, and scientific analyses and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us or our affiliates. **In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and product candidates.** Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be valid or enforceable or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. Patent applications in the U. S. are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the U. S. Patent and Trademark Office (the " USPTO ") for the entire time prior to issuance as a U. S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors or co- owners were the first to invent, or the first to file patent applications on, our drug candidates or their use as drugs. In the event that a third party has also filed a U. S. patent application relating to our drug candidates or a similar invention, we may have to participate in interference or derivation proceedings declared by the USPTO to determine priority of invention in the U. S. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a loss of our U. S. patent position. Furthermore, we may not have identified all U. S. and non- U. S. patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies. Composition- of- matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our patent applications covering composition- of- matter of our drug candidates will be considered patentable by the USPTO and courts in the U. S. or by the patent offices and courts in other countries, nor can we be certain that the claims in our issued composition- of- matter patents will not be found invalid or unenforceable if challenged. Method- of- use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products " off- label. " Although off- label prescriptions may infringe or contribute to the infringement of method- of- use patents, the practice is common and such infringement is difficult to prevent or prosecute. We cannot guarantee that any of our patent searches or analyses, including 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 third- party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our drug candidates in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent' s prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third- party patent or may incorrectly predict whether a third- party' s pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our drug candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products. We may be subject to a third- party preissuance submission of prior art to the USPTO and foreign patent agencies, or become involved in opposition, derivation, reexamination, inter partes review, post- grant review, or other patent office proceedings or litigation, in the U. S. or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Any failure to obtain or maintain patent protection with respect to our drug

candidates could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is costly, time- consuming, and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs, and may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. Recent patent reform legislation in the United States and other countries, including the Leahy- Smith America Invents Act, or the Leahy- Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost- effective avenues for competitors to challenge the validity of patents. These include allowing third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. After March 2013, under the Leahy- Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third ~~-~~party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our drug candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor' s patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. 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, financial condition, results of operations, and / or growth prospects. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by Congress, the federal courts, the USPTO and the relevant law- making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict how future decisions by Congress, the federal courts or the USPTO may impact the value of our patents. Obtaining and maintaining our 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 on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Although an inadvertent lapse, including due to the effect of **geopolitical conflict** ~~the COVID- 19 pandemic~~ on us or our patent maintenance vendors, can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance 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. Noncompliance events that could result in abandonment or lapse of a patent or patent application or invalidity of an issued patent include failure to respond to official actions within prescribed time limits, non- payment of fees, failure to properly legalize and submit formal documents, and failure to submit certain prior art. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business. The lives of our patents may not be sufficient to effectively protect our products and business. Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing, and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such drug candidates are commercialized. Even if patents covering our drug candidates are obtained, once a patent covering a drug candidate has expired, we may be open to competition, including biosimilar or generic medications. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug candidates similar or identical to ours. Our patents issued as of December 31, ~~2022~~ **2023**, are anticipated to expire on dates ranging from ~~2023~~ **2024** to 2042, subject to any patent extensions that may be available for such patents. If patents are issued on our patent applications pending as of December 31, ~~2022~~ **2023**, the resulting patents are projected to expire on dates ranging from 2025 to ~~2042~~ **2044**. In addition, although upon issuance in the United States a patent' s life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each first regulatory review period for a product, and any patent can be extended only once, for a

single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may be subject to claims that former employees, collaborators, or other third parties have an interest in our patents or other intellectual property as an inventor or co- inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our drug candidates. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. We or our licensors may have relied on third- party consultants or collaborators or on funds from third parties, such as the U. S. government, such that we or our licensors are not the sole and exclusive owners of the patents we in- licensed. If other third parties have ownership rights or other rights to our patents, including in- licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self- executing, or the assignment agreements **have been, and** may be **,** breached, and we **have been, and** may be **,** forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. **We may not have adequate remedies for any breach of our assignment agreements or related claims.** Such claims **related to the ownership of what we regard as our intellectual property** could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects. We may not be able to protect our intellectual property rights throughout the world. Patents are of national or regional effect, and filing, prosecuting, maintaining, and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can have a different scope and strength than do those in the United States. In addition, the laws of some foreign countries, particularly certain developing countries, do not currently, or may not in the future, 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, 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 obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing. We license patent rights from third- party owners. Such licenses may be subject to early termination if we fail to comply with our obligations in our licenses with third parties, which could result in the loss of rights or technology that are material to our business. We are a party to licenses that give us rights to third- party intellectual property or technology that is necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements we are obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. In addition, under certain of such agreements, we are required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations, including due to ~~the impact of the COVID- 19 pandemic on our business operations or~~ our use of the intellectual property licensed to us in an unauthorized manner, and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business, harming our ability to develop, manufacture, and / or commercialize our platform or drug candidates. In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant

agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and / or growth prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. Our business also would suffer if any current or future licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor' s rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant research programs or drug candidates and our business, financial condition, results of operations, and / or growth prospects could suffer. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those relating to: • the scope of rights granted under the license agreement and other interpretation- related issues; • whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement; • our right to sublicense patent and other rights to third parties under collaborative development relationships; • whether we are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our drug candidates, and what activities satisfy those diligence obligations; • the priority of invention of patented technology; • the amount and timing of payments owed under license agreements; and • the allocation of ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer. We depend, in part, on our licensors to file, prosecute, maintain, defend, and enforce patents and patent applications that are material to our business. If the licensor retains control of prosecution of the patents and patent applications licensed to us, we may have limited or no control over the manner in which the licensor chooses to prosecute or maintain its patents and patent applications and have limited or no right to continue to prosecute any patents or patent applications that the licensor elects to abandon. If our licensors or any future licensees having rights to file, prosecute, maintain, and defend our patent rights fail to conduct these activities for patents or patent applications covering any of our drug candidates, including due to the impact of **geopolitical conflict** ~~the COVID- 19 pandemic~~ on our licensors' business operations, our ability to develop and commercialize those drug candidates may be adversely affected and we may not be able to prevent competitors from making, using, or selling competing products. We cannot be certain that such activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. We may wish to form collaborations in the future with respect to our drug candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans. Our drug candidates may also require specific components to work effectively and efficiently, and rights to those components may be held by others. We may be unable to in- license any compositions, methods of use, processes or other third - party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which would harm our business. If we fail to obtain licenses to necessary third- party intellectual property rights, we may need to cease use of the compositions or methods covered by such third- party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Any delays in entering into new collaborations or strategic partnership agreements related to our drug candidates could delay the development and commercialization of our drug candidates in certain geographies, which could harm our business prospects, financial condition, and results of operations. The licensing and acquisition of third- party intellectual property rights is a competitive

practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third- party intellectual property rights that we may consider necessary or attractive in order to commercialize our drug candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional drug candidates that we may seek to acquire. Moreover, some of our owned and in- licensed patents or patent applications or future patents are or may be co- owned with third parties. If we are unable to obtain an exclusive license to any such third- party co- owners' interest in such patents or patent applications, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co- owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in- licensed patents may be subject to a reservation of rights by one or more third parties. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects. Litigation regarding patents, patent applications, and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate. Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third- party claims of intellectual property infringement related to our drug candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post- grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post- grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. Other parties may hold or obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization. Furthermore, patent reform and changes to patent laws add uncertainty to the possibility of challenge to our patents in the future. We cannot assure you that our drug candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties. In addition, third parties may challenge our existing or future patents. Competitors may also infringe our patents or other intellectual property or the intellectual property of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time- consuming and divert the time and attention of our management and scientific personnel. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding: • the patentability of our inventions relating to our drug candidates; and / or • the enforceability, validity or scope of protection offered by our patents relating to our drug candidates; and / or • findings that our drug candidates, products, or activities infringe third - party patents or other intellectual property rights. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business including distracting our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. 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. Third parties asserting their patent or other intellectual property rights against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our drug candidates or force us to cease some of our business operations. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, cause development delays, and may impact our reputation. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. In the event we are able to establish third- party infringement of our patents, 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. Furthermore, 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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action, or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non- infringing technology, fail to defend an infringement action successfully, or have infringed patents declared invalid, we may: • incur substantial monetary damages, including treble damages and attorneys' fees for willful infringement; • obtain one or more licenses from third parties and potentially pay royalties; • redesign our infringing products, which may be impossible on a cost- effective basis or require substantial time and monetary expenditure; • encounter significant delays in bringing our drug candidates to market; and / or • be precluded from participating in the manufacture, use, or sale of our drug candidates or methods of treatment requiring licenses. In that event, we would be unable to further develop and commercialize our drug candidates, which could harm our business significantly. If our trademarks and trade names are not adequately protected, then

we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our current or future trademarks or trade names may be challenged, infringed, circumvented, declared generic or descriptive, or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Moreover, any name we have proposed to use with our drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. We may be unable to adequately prevent disclosure of trade secrets and other proprietary information. We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable; however, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third- party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In addition, others may independently discover our trade secrets and proprietary information, and we would have no right to prevent them from using that technology or information to compete with us. Costly and time- consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition. We may be subject to claims that our employees, collaborators, partners, contractors, or advisors have wrongfully used or disclosed alleged trade secrets of third parties. Many of our employees were previously employed at universities, Elan or Elan subsidiaries, or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Likewise, our collaborators, partners, contractors, and advisors may have in the past, or may currently, work with or for universities, or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know- how of third parties is not disclosed to us or used in their work for us, we may be subject to claims that we or our employees, collaborators, partners, contractors, or advisors have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate, be derived from, or benefited from the knowledge of the trade secrets or other proprietary information of third parties. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection

afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make drug candidates that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that our pending patent applications will not lead to issued patents; • issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in- license will result in issued patents with claims that cover our drug candidates or uses thereof in the United States or in other foreign countries; • the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties; • if enforced, a court may not hold that our patents are valid, enforceable and infringed; • we may need to initiate litigation or administrative proceedings to enforce and / or defend our patent rights which will be costly whether we win or lose; • we may choose not to file a patent in order to maintain certain trade secrets or know- how, and a third party may subsequently file a patent covering such intellectual property; • we may fail to adequately protect and police our trademarks and trade secrets; and • the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications. Should any of these events occur, they could significantly harm our business, results of operations, and prospects. Risks Related to Our Ordinary Shares The market price of our ordinary shares may fluctuate widely. Our ordinary shares commenced trading on the Nasdaq Global Market on December 21, 2012 and currently trade on the Nasdaq Global Select Market. We cannot predict the prices at which our ordinary shares may trade. The market price of our ordinary shares may fluctuate widely, depending upon many factors, some of which may be beyond our control, including: • our ability to obtain financing as needed; • progress in and results from our ongoing or future nonclinical research and clinical trials; • the execution of our agreements with third parties, including with Roche, BMS, and Novo Nordisk; • failure or delays in advancing our nonclinical drug candidates or other drug candidates we may develop in the future into clinical trials; • results of clinical trials conducted by others, including on drugs that would compete with our drug candidates; • issues in manufacturing our drug candidates; • regulatory developments or enforcement in the U. S. and other countries; • developments or disputes concerning patents or other proprietary rights; • introduction of technological innovations or new commercial products by our competitors; • changes in estimates or recommendations by securities analysts, if any, who cover our company; • public concern over our drug candidates; • litigation; • future sales of our ordinary shares by us or by existing shareholders; • general market conditions; • changes in the structure of healthcare payment systems; • failure of any of our drug candidates, if approved, to achieve commercial success; • economic and other external factors or other disasters or crises; • period- to- period fluctuations in our financial results; • overall fluctuations in U. S. equity markets; • our quarterly or annual results, or those of other companies in our industry; • announcements by us or our competitors of significant acquisitions or dispositions; • the operating and ordinary share price performance of other comparable companies; • investor perception of our company and the drug development industry; • natural or environmental disasters that investors believe may affect us; • changes in tax laws or regulations applicable to our business or the interpretations of those tax laws and regulations by taxing authorities; or • fluctuations in the budgets of federal, state and local governmental entities around the world. These and other external factors may cause the market price and demand for our ordinary shares to fluctuate substantially, which may limit or prevent investors from readily selling their ordinary shares and may otherwise negatively affect the liquidity of our ordinary shares. In particular, stock markets in general have experienced volatility that has often been unrelated to the operating performance of a particular company. These broad market fluctuations may adversely affect the trading price of our ordinary shares. Some companies that experienced volatility in the trading price of their stock have been the subject of securities class action litigation. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management. Your percentage ownership in Prothena may be diluted in the future. As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions (including the sale of ordinary shares pursuant to our December 2021 Distribution Agreement **, as may be amended from time to time, and as discussed below**), or otherwise. We may need to raise additional capital in the future. If we are able to raise additional capital, we may issue equity or convertible debt instruments, which may severely dilute your ownership interest in us. In addition, we intend to continue to grant option awards to our directors, officers and employees, which would dilute your ownership stake in us. As of December 31, ~~2022~~ **2023** , the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plans was ~~12~~ **13** , ~~618~~ **477** , ~~591~~ **039** . If we are unable to maintain effective internal controls, our business could be adversely affected. We are subject to the reporting and other obligations under the U. S. Securities Exchange Act of 1934, as amended, including the requirements of Section 404 of the U. S. Sarbanes- Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting. In addition, under Section 404 (b) of the U. S. Sarbanes- Oxley Act, if we are either an " accelerated filer " or " large accelerated filer, " our independent registered public accounting firm must attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of

its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes- Oxley Act. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources. Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with accounting principles generally accepted in the U. S. During the course of our review and testing of our internal controls, we **have identified, and** may identify **in the future,** deficiencies and **may** be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our consolidated financial statements may be materially misstated. We, or our independent registered public accounting firm (if required), may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. We cannot provide assurance that a material weakness will not occur in the future, or that we will be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 and the related rules and regulations of the SEC when required. A material weakness in internal control over financial reporting is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company' s annual or interim consolidated financial statements will not be prevented or detected on a timely basis by the company' s internal controls. If we cannot in the future favorably assess, or our independent registered public accounting firm (if required), is unable to provide an unqualified attestation report on, the effectiveness of our internal controls over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on our share price. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would have an adverse effect on our business, financial position and results of operations. If we were treated as a passive foreign investment company for U. S. federal income tax purposes, it could result in adverse U. S. federal income tax consequences to United States holders of our ordinary shares. Significant potential adverse U. S. federal income tax implications generally apply to U. S. investors owning shares of a passive foreign investment company (" PFIC "), directly or indirectly. In general, we would be a PFIC for a taxable year if either (i) 75 % or more of our income constitutes passive income, or (ii) 50 % or more of our assets produce passive income or are held for the production of passive income. Changes in the composition of our active or passive income, passive assets or changes in our fair market value may cause us to become a PFIC. A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each taxable year). We do not believe we were a PFIC for U. S. federal income tax purposes for our taxable year ended December 31, ~~2022~~ **2023** . However, the application of the PFIC rules is subject to uncertainties in a number of respects, and we cannot assure that the U. S. Internal Revenue Service (the " IRS ") will not take a contrary position. We also cannot assure that we will not be a PFIC for U. S. federal income tax purposes for the current taxable year or any future taxable year. We may not be able to successfully maintain our tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects. We are incorporated in Ireland and maintain subsidiaries or offices in Ireland and the U. S. We are able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax- efficient jurisdictions, together with intra- group service agreements. However, changes in tax laws or interpretations thereof in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the IRS and the Irish Revenue Commissioners (" Irish Revenue "), actively audit and otherwise challenge these types of arrangements, and have done so in our industry. We are subject to reviews and audits by the IRS, Irish Revenue and other taxing authorities from time to time, and the IRS, Irish Revenue or other taxing authority may challenge our structure and inter- group arrangements. Responding to or defending against challenges from taxing authorities could be expensive and time consuming, and could divert management' s time and focus away from operating our business. We cannot predict whether and when taxing authorities will conduct an audit, challenge our tax structure or the cost involved in responding to any such audit or challenge. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, all of which could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. **In addition to the impact on changes in tax laws, our provision for income tax can be materially impacted, for example, by the geographical mix of our profits and losses, changes in our business, such as internal restructuring and acquisitions, changes and accounting guidance and other regulatory, legislative or judicial developments changes in tax rates, tax audit determinations, changes in our uncertain tax positions, changes in our intent and capacity to permanently reinvest foreign earnings, changes to our transfer pricing practices, tax deductions attributed to equity compensation and changes in our need for a valuation allowance for deferred tax assets.** Future changes to the tax laws relating to multinational corporations could adversely affect us. Under current law, we are treated as a foreign corporation for U. S. federal tax purposes. However, changes to the U. S. Internal Revenue Code, U. S. Treasury Regulations or other IRS guidance thereunder could adversely affect our status as a foreign corporation or otherwise affect our effective tax rate. For example, in 2017 the United States enacted tax reform that contained significant changes to corporate taxation, including a provision that requires capitalization and amortization of research and development costs over five years for tax years beginning after December 31, 2021. In addition, the Irish Government, Irish Revenue, U. S. Congress, the IRS, the Organization for Economic Co- operation and Development **(" OECD ")** , and other governments and agencies in jurisdictions where we do business have recently focused on issues related to the taxation of multinational corporations, **including** ~~and specifically in~~ the ~~area of "~~ **OECD' s Global Anti-** ~~base~~ **Base** ~~erosion~~ **Erosion** ~~and profit shifting~~ **Model Rules (Pillar Two)** , ~~" such as where payments are made between affiliates from~~ **which apply a 15 % global minimum tax rate on** a jurisdiction **- by- jurisdiction basis to**

groups with ~~high tax rates~~ **turnover of not less than € 750 million in at least** ~~to~~ **two** ~~a jurisdiction~~ **of the four prior fiscal years. Pillar Two has been implemented into Irish law** with ~~lower tax rates~~ **effect for periods beginning on or after December 31, 2023** . As a result **of Pillar Two or other policy changes, whether at national or supranational level** , the tax laws in Ireland, the U. S., and other countries in which we do business could change on a prospective or retroactive basis, and any such changes could have an adverse effect on our business, financial condition, results of operations, and / or growth prospects. Irish law differs from the laws in effect in the United States and may afford less protection to holders of our ordinary shares. It may not be possible to enforce court judgments obtained in the U. S. against us in Ireland based on the civil liability provisions of the U. S. federal or state securities laws. In addition, there is uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U. S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U. S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U. S. currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U. S. federal or state court based on civil liability, whether or not based solely on federal or state securities laws, would not automatically be enforceable in Ireland. As an Irish incorporated company, we are governed by the Irish Companies Act 2014, as amended (the " Companies Act "), which differs in some material respects from laws generally applicable to U. S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our ordinary shares may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the U. S. The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares. Under the Irish Takeover Panel Act, 1997, Takeover Rules, 2022 (the " Irish Takeover Rules "), if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30 % or more of the voting rights of the company, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30 % and 50 % of the voting rights in the company if the effect of such acquisition were to increase that person' s percentage of the voting rights by 0. 05 % within a 12 month period. Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and " controlled companies " are presumed to be acting in concert with any corporate shareholder who holds 20 % or more of our shares. The application of these presumptions may result in restrictions upon the ability of any of the concert parties and / or members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. In the future, we may consult with the Irish Takeover Panel with respect to the application of this presumption and the restrictions on the ability to acquire further securities, although we are unable to provide any assurance as to whether the Irish Takeover Panel will overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares. Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors. We are subject to the Irish Takeover Rules, pursuant to which our Board is not permitted to take any action that might frustrate an offer for our ordinary shares once our Board has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of ordinary shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business, or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our Board has reason to believe an offer is or may be imminent. These provisions may give our Board less ability to control negotiations with hostile offerors and protect the interests of holders of ordinary shares than would be the case for a corporation incorporated in a jurisdiction of the U. S. Irish law requires that our shareholders renew every five years the authority of our Board of Directors to issue shares and to do so for cash without applying the statutory pre- emption right, and if our shareholders do not renew these authorizations by May 17, 2027 (or any renewal is subject to limitations), our ability to raise additional capital to fund our operations would be limited. As an Irish incorporated company, we are governed by the Companies Act. The Companies Act requires that every five years our shareholders renew the separate authorities of our Board to (a) allot and issue shares, and (b) opt out of the statutory pre- emption right that otherwise applies to share issuances for cash (which pre- emption right would require that shares issued for cash be offered to our existing shareholders on a pro rata basis before the shares may be issued to new shareholders). At our shareholders' annual general meeting held on May 17, 2022, our shareholders authorized our Board to issue ordinary shares up to the amount of our authorized share capital, and to opt out of the statutory pre- emption right for such issuances. Under Irish law, these authorizations will expire on May 17, 2027, five years after our shareholders last renewed these authorizations. Irish law requires that our shareholders renew the authority for our Board to issue ordinary shares by a resolution approved by not less than 50 % of the votes cast at a general meeting of our shareholders. Irish law requires that our shareholders renew the authority of our Board to opt out of the statutory pre- emption right in share issuances for cash by a resolution approved by not less than 75 % of the votes cast at a general meeting of our shareholders. If these authorizations are not renewed before May 17, 2027, or are renewed with limitations, our Board would be limited in its ability to issue shares, which would limit our ability to raise additional capital to fund our operations, including the research, development and potential commercialization of our drug candidates. Transfers of our ordinary shares may be subject

to Irish stamp duty. Irish stamp duty may be payable in respect of transfers of our ordinary shares (currently at the rate of 1 % of the price paid or the market value of the shares acquired, if greater). Under the Irish Stamp Duties Consolidation Act, 1999 (the " Stamp Duties Act "), a transfer of our ordinary shares from a seller who holds shares through The Depository Trust Company (" DTC ") to a buyer who holds the acquired shares through DTC ~~should~~ **will** not be subject to Irish stamp duty. Shareholders may also transfer their shares into or out of DTC without giving rise to Irish stamp duty provided that there is no change in the beneficial ownership of such shares and the transfer into or out of DTC is not effected in contemplation of a subsequent sale of such shares to a third party; in order to benefit from this exemption from Irish stamp duty, the seller must confirm to us that there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and there is no agreement for the sale of the shares by the beneficial owner to a third party being contemplated. A transfer of our ordinary shares (i) by a seller who holds shares outside of DTC to any buyer, or (ii) by a seller who holds the shares through DTC to a buyer who holds the acquired shares outside of DTC, may be subject to Irish stamp duty. Payment of any Irish stamp duty is generally a legal obligation of the transferee. Any Irish stamp duty payable on transfers of our ordinary shares could adversely affect the price of those shares. We do not anticipate paying cash dividends, and accordingly, shareholders must rely on ordinary share appreciation for any return on their investment. We anticipate losing money for the foreseeable future and, even if we do turn a profit, we do not anticipate declaring or paying any cash dividends for the foreseeable future. Therefore, the success of an investment in our ordinary shares will depend upon appreciation in their value and in order to receive any income or realize a return on your investment, you will need to sell your Prothena ordinary shares. There can be no assurance that our ordinary shares will maintain their price or appreciate in value. Dividends paid by us may be subject to Irish dividend withholding tax. Although we do not currently anticipate paying cash dividends, if we were to do so in the future, a dividend withholding tax (currently at a rate of 25 %) may arise. A number of exemptions from dividend withholding tax exist such that shareholders resident in the U. S. and shareholders resident in other countries that have entered into a double taxation treaty with Ireland may be entitled to exemptions from dividend withholding tax subject to the completion of certain dividend withholding tax declaration forms. Shareholders entitled to an exemption from Irish dividend withholding tax on any dividends received from us will not be subject to Irish income tax in respect of those dividends, unless they have some connection with Ireland other than their shareholding (for example, they are resident in Ireland). Non- Irish resident shareholders who receive dividends subject to Irish dividend withholding tax will generally have no further liability to Irish income tax on those dividends. Prothena ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax. Irish capital acquisitions tax (" CAT ") could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT. Gifts and inheritances passing between spouses are exempt from CAT. It is recommended that each shareholder consult his or her own tax advisor as to the tax consequences of holding our ordinary shares or receiving dividends from us.