**Risk Factors Comparison 2024-03-06 to 2023-03-23 Form: 10-K**

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You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10- K, including the section of this report titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations " and our financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this Annual Report on Form 10- K occurs, our business, operating results and financial condition could be seriously harmed and the trading price of our ordinary shares could decline. This Annual Report on Form 10- K also contains forward- looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward- looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10- K. Risks Related to Our Financial Results and Capital Requirements We are a clinical- stage **biotechnology** ~~genetic medicines~~ company with a history of losses, and we expect to continue to incur losses for the foreseeable future, and we may never achieve or maintain profitability. We are a clinical- stage **biotechnology** ~~genetic medicines~~ company and have incurred significant operating losses since our incorporation in 2012. Our net loss was $ **57. 5 million and $** 161. 8 ~~million and $ 122. 2~~ million for the fiscal years ended December 31, **2023 and** 2022 ~~and 2021~~, respectively. As of December 31, **2023 and** 2022 ~~and 2021~~, we had an accumulated deficit of $ **1, 024. 9 million and $** 967. 3 ~~million and $ 805. 5~~ million, respectively. To date, we have not generated any product revenue. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We ~~currently have no products~~ **are a clinical- stage biotechnology company focused** on **unlocking the broad potential of RNA medicines (also known as oligonucleotides), or** ~~the~~ **those** ~~market~~ **targeting ribonucleic acid (RNA), to transform human health. Our RNA medicines platform, PRISMTM, combines multiple modalities, chemistry innovation** and ~~expect~~ **deep insights into human genetics to deliver scientific breakthroughs** that **treat both rare** ~~it may be many years, if ever, before we have a product candidate ready for commercialization. We have a robust~~ and ~~diverse pipeline~~ **prevalent disorders. Our toolkit** of ~~PN~~ **RNA** - **targeting modalities includes RNA** ~~modified, stereopure oligonucleotides, including programs using our~~ editing, splicing, ~~and~~ **antisense** silencing ~~modalities~~ **and RNA interference, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology**. Our lead ~~clinical~~ programs are ~~focused~~ in ~~,~~ **rare** and **prevalent** ~~aim to address, muscle~~ diseases **, including alpha- 1 antitrypsin deficiency** ( **" AATD "), obesity, Duchenne muscular dystrophy (" DMD " – splicing** ), ~~hepatic~~ **and Huntington' s** ~~diseases~~ – **disease** ( ~~" AATD – editing), and CNS diseases (~~HD **"** ~~, ALS and FTD – silencing~~ ). We have not generated, and do not expect to generate, any product revenue for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, manufacturing, preclinical studies and clinical trials and the regulatory review process for product candidates. The amount of future losses is uncertain. To achieve profitability, we must successfully develop product candidates, obtain regulatory approvals to market and commercialize product candidates, manufacture any approved product candidates on commercially reasonable terms, establish a sales and marketing organization or suitable third- party alternatives for any approved product and raise sufficient funds to finance our business activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause our shareholders to lose all or part of their investment. We will require substantial additional funding, which may not be available on acceptable terms, or at all. We have used substantial funds to develop our programs and PRISM, our proprietary discovery and drug development platform, and will require substantial funds to conduct further research and development, including preclinical studies and clinical trials of our product candidates, seek regulatory approvals for our product candidates and manufacture and market any products that are approved for commercial sale. We believe that our existing cash and cash equivalents will be sufficient to fund our operations for at least the next 12 months. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. We do not expect to realize any appreciable revenue from product sales or royalties in the foreseeable future, if at all. Our revenue sources will remain extremely limited unless and until our product candidates complete clinical development and are approved for commercialization and successfully marketed. Because we cannot be certain of the length of time or activities associated with successful development and commercialization of our product candidates, we are unable to estimate the actual funds we will require to develop and commercialize them. Our future capital requirements will depend on many factors, including, but not limited to, the following: • our monthly spending levels, based on new and ongoing development and corporate activities; • the scope, progress, results and costs of drug discovery, preclinical and clinical development for our product candidates; • our ability to establish and maintain collaboration arrangements, and whether our collaboration partners decide to exercise option rights in connection with targets and development programs; • the costs, timing and outcome of regulatory review of our product candidates; • our ability to obtain marketing approval for our product candidates; • the impacts of **any local or** ~~the COVID- 19~~ global ~~pandemic (~~ **health issues, the conflict involving Russia** and ~~emerging~~ **Ukraine, the conflict in the Middle East, global economic uncertainty, rising inflation, rising interest rates** or **market disruptions** ~~future variants of COVID- 19)~~ on our business; • the achievement of milestones and other development targets that trigger payments under our agreements with our key collaboration partners, or any other strategic collaborations into

which we may enter ~~; • the extent to which we are obligated to reimburse clinical trial costs or expenses and other costs and expenses associated with clinical activities under our agreements with our key collaboration partners, or any other future collaboration agreements, if any~~ ; • the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval; • market acceptance of our product candidates, to the extent any are approved for commercial sale, and the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; • the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property- related claims; • the costs of securing manufacturing arrangements internally or with third parties for drug supply. To date, we have primarily financed our operations through sales of our securities and our collaborations with third parties. Through December 31, ~~2022~~ **2023** , we have received an aggregate of approximately $ 1, ~~021~~ **295** . ~~2~~ **1** million in net proceeds from these transactions, consisting of $ ~~630~~ **727** . ~~9~~ **6** million in net proceeds from public and other registered offerings of our ordinary shares, $ ~~301~~ **478** . ~~0~~ **2** million from our collaborations, exclusive of any potential future milestone and royalty payments, and $ 89. 3 million in net proceeds from private placements of our debt and equity securities. ~~Subsequent to~~ **In January 2024, the representatives of the underwriters in connection with the previously disclosed underwritten public offering (the "** December ~~31, 2022~~ **2023 Offering ") exercised their option to purchase an additional 3** , ~~we received~~ **000, 000 ordinary shares as a part of the December 2023 Offering, for additional net proceeds of approximately** $ ~~170~~ **14** . 0 million ~~in cash, of which $ 120. 0 million was an upfront payment under the GSK Collaboration Agreement and $ 50. 0 million was under the GSK Equity Investment~~ . On March 3, 2022, we filed a new universal shelf registration on Form S- 3 with the SEC, which was declared effective by the SEC on May 4, 2022, pursuant to which we registered for sale up to $ 500. 0 million of any combination of our ordinary shares, debt securities, warrants, rights and / or units from time to time and at prices and on terms that we may determine, which we refer to as the " 2022 Form S- 3. " The 2022 Form S- 3 includes a prospectus covering up to approximately $ 132. 0 million in ordinary shares that had not yet been issued or sold under our Sales Agreement with Jefferies LLC (" Jefferies ") for our " at- the- market " equity program. As of March ~~22~~ **1** , ~~2023~~ **2024** , we have $ ~~430~~ **311** . ~~0~~ **7** million in securities available for issuance under the 2022 Form S- 3, including approximately $ ~~132~~ **128** . ~~0~~ **7** million in ordinary shares available for issuance under our at- the- market equity program. As of March ~~22~~ **1** , ~~2023~~ **2024** , we have received approximately $ ~~118~~ **121** . ~~0~~ **3** million in gross proceeds from our at- the- market equity program. We intend to seek additional funding in the future through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these financing sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. We may seek access to the capital and credit markets for working capital, capital expenditure, and other business initiatives. The capital and credit markets have experienced extreme volatility and disruption, which may lead to uncertainty and liquidity issues for both borrowers and investors. In the event of adverse market conditions, or other factors, additional funds may not be available to us on acceptable terms or at all. For example, the global economy has been experiencing ~~increasing~~ interest ~~rates~~ **rate increases** and **higher** inflation, which could negatively impact our business and our ability to raise additional funds. If we raise additional funds by issuing equity or convertible debt securities, our shareholders will suffer dilution and the terms of any financing may adversely affect the rights of our shareholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing shareholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities ~~received~~ **receive** any distribution of corporate assets. If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, limit or terminate our research and development programs and preclinical studies or clinical trials, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our product candidates or technologies that we would otherwise pursue on our own. Our business may be impacted by macroeconomic conditions, including fears concerning the financial services industry, inflation, rising interest rates and volatile market conditions, and other uncertainties beyond our control. Actual events involving limited liquidity, defaults, non- performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market- wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank failed and was taken into receivership by the Federal Deposit Insurance Corporation; on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership; the following week, a syndicate of U. S. banks infused $ 30 billion in First Republic Bank; and later that same week, the Swiss Central Bank provided $ 54 billion in covered loan and short- term liquidity facilities to Credit Suisse Group AG, all in an attempt to reassure depositors and calm fears of a banking contagion. Our ability to effectively run our business could be adversely affected by general conditions in the global economy and in the financial services industry. Various macroeconomic factors could adversely affect our business, including fears concerning the banking sector, changes in inflation, interest rates and overall economic conditions and uncertainties. A severe or prolonged economic downturn could result in a variety of risks, including our ability to raise additional funding on a timely basis or on acceptable terms. A weak or declining economy could also impact third parties upon whom we depend to run our business. ~~Increasing concerns~~ **Concerns** over bank failures and bailouts and their potential broader effects and potential systemic risk on the banking sector generally and on the biotechnology industry and its participants may adversely affect our access to capital and our business and operations more generally. Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have arrangements directly, or the financial services industry or economy in general **.** Our

management has broad discretion over the use of proceeds received from sales of our securities and our collaborations with third parties and the proceeds may not be used effectively. Our management has broad discretion as to the use of proceeds we receive from conducting sales of our securities and our collaborations with third parties and could use the proceeds for purposes other than those contemplated at the time of such transactions. It is also possible that the proceeds we have received, or may receive, from securities sales and collaborations will be invested in a way that does not yield a favorable, or any, return for us. Our ~~short~~ operating history **as a clinical- stage biotechnology company** may make it difficult for shareholders to evaluate the success of our business to date and to assess our future viability. We are a clinical- stage ~~genetic~~ **biotechnology company focused on unlocking the broad potential of RNA** medicines ~~company~~ **(also known as oligonucleotides), or those targeting ribonucleic acid (RNA), to transform human health. Our RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Our toolkit of RNA- targeting modalities includes RNA editing, splicing, antisense silencing and RNA interference, providing us** with **unique capabilities for designing** ~~a limited operating history. We commenced active operations in 2012. Our operations to date have primarily included research~~ and **sustainably delivering candidates that optimally address disease biology** ~~development activities, manufacturing, preclinical and clinical development, patient advocacy activities, business planning and raising capital. We have a robust and diverse pipeline of PN- modified, stereopure oligonucleotides, including programs using our editing, splicing, and silencing modalities~~. Our lead ~~clinical~~ programs are ~~focused~~ in ~~,~~ **rare** and **prevalent** ~~aim to address, muscle~~ diseases ~~(~~**, including AATD, obesity,** DMD ~~– splicing)~~, ~~hepatic diseases (AATD – editing),~~ and ~~CNS diseases (~~HD ~~, ALS and FTD – silencing)~~. We have not yet demonstrated our ability to successfully complete pivotal clinical trials, obtain marketing approvals, or conduct sales and marketing activities necessary for successful product commercialization. We have limited experience manufacturing our products at commercial scale or arranging for a third party to do so on our behalf. Typically, it takes many years to develop and commercialize a therapeutic from the time it is discovered to when it is available for treating patients. Further, drug development is a capital- intensive and highly speculative undertaking that involves a substantial degree of risk. You should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by biotechnology companies in the early stages of clinical development, such as ours. Any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. We, or third parties upon whom we depend, may face risks related to **local and global** health epidemics ~~, including the COVID- 19 pandemic and variants thereof~~, which may delay our ability to complete our ongoing clinical trials, initiate additional clinical trials, delay regulatory activities and have other adverse effects on our business and operations ~~. Since December 2019, multiple countries throughout the world and their economies, including the United States, have been subject to intermittent shutdowns and adversely affected by the COVID- 19 global pandemic. We are continuing to evaluate any continued impacts from the global pandemic and the extent to which any responsive measures may materially and adversely affect our business operations and financial condition~~. As a clinical- stage company with multiple programs and multiple clinical trials currently underway, ~~the pandemic is~~ **any local or global health issues could** ~~impacting~~ **impact** the execution of our clinical trials. **For example, beginning in March 2020, multiple countries throughout the world and their economies, including the United States, were subject to intermittent shutdowns and were adversely affected by the COVID- 19 global pandemic.** We ~~have~~ **had** clinical trial sites located in countries that ~~have~~ **had** been affected by COVID- 19 and variants thereof. Clinical site initiation and patient enrollment **was** ~~has been~~ delayed due to prioritization of hospital resources in favor of COVID- 19 patients and difficulties in recruiting clinical site investigators and clinical site staff. Some patients ~~have~~ **were** not ~~been~~ able to travel or gain access to clinical trial sites due to local restrictions. Similarly, our ability to recruit and retain patients and principal investigators and site staff ~~who, as~~ **was** ~~healthcare providers, may have heightened risk of exposure to COVID- 19, has been~~ negatively impacted, which ~~has~~ delayed the timelines of our clinical trial operations. We rely upon third parties for many aspects of our business, including the raw materials used to make our product candidates and the conduct of our clinical trials and preclinical studies. While we have built up inventory to assist us through this uncertain operating environment, our suppliers may be disrupted now or in the future **due to a local or global health epidemic** , which ~~may~~ **could** affect our ability to procure items that are essential for our research and development activities and ~~may~~ **could** cause ~~pricing~~ increases **to our costs** , inflation, and significant disruptions to our business. ~~The COVID- 19 global pandemic, including any emerging variants of COVID- 19, is continuing to evolve and is subject to change.~~ While we have adapted our processes to lessen the impact **of a potential local or global health epidemic** ~~that COVID- 19, and variants thereof,~~ may have on our business, any potential delays or long- term impacts on our business, our clinical trials, healthcare systems or the global economy ~~are~~ **could be** highly uncertain. These effects ~~may~~ **could** materially adversely affect our business, financial condition, results of operations, and prospects. Risks Related to the Discovery, Manufacturing, Development and Commercialization of Our Product Candidates The approach we are taking to discover and develop ~~oligonucleotides~~ **RNA medicines** is novel and may never lead to marketable products. We have concentrated our efforts and research and development activities on **RNA medicines (also known as** oligonucleotides **)** and enhancing PRISM, our proprietary discovery and drug development platform. PRISM enables us to target genetically defined diseases with stereopure oligonucleotides across multiple therapeutic modalities. Our future success depends on the successful development of ~~stereopure oligonucleotides~~ **our RNA medicines** and the effectiveness of PRISM. The scientific discoveries that form the basis for our efforts to discover and develop new product candidates, including our discoveries about the relationships between oligonucleotide stereochemistry and pharmacology, are relatively new. **Our** ~~We use~~ PRISM **platform combines multiple modalities** ~~to screen candidates and optimize pharmacologic profiles based on predefined design principles~~ , ~~which reflect a~~ **chemistry innovation and** deep ~~understanding of how the interplay among oligonucleotide sequence, chemistry~~ **insights into human genetics to deliver scientific breakthroughs that treat both rare** and **prevalent disorders** ~~backbone stereochemistry impacts key pharmacological properties~~ . The scientific evidence to support the feasibility of developing

medicines based on ~~these~~ **our** discoveries is limited **,** ~~. Skepticism~~ as **we** ~~to the feasibility of developing oligonucleotides generally has been, and may continue to be, expressed in scientific literature. In addition, decisions by other companies with respect to their oligonucleotide development efforts may increase skepticism in the marketplace regarding the potential for oligonucleotides. A number of clinical trials for oligonucleotide products conducted by other companies~~ have not ~~been~~ **yet completed** successful ~~, but some have received regulatory approval. The pharmacological properties ascribed to the investigational compounds we are testing in laboratory studies may not be positively demonstrated in~~ clinical ~~trials in patients, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. If our product candidates prove to be ineffective, unsafe or commercially unviable, PRISM and our pipeline would have little, if any, value, which would substantially harm our business, financial condition, results of operations and prospects. In addition, our approach, which focuses on using oligonucleotides for drug~~ development **of** ~~, as opposed to multiple or other, more advanced proven technologies, and~~ **an** ~~new products and technologies that may enter the market, may expose us to additional financial risks and make it more difficult to raise additional capital if we are not successful in developing one or more oligonucleotides~~ **oligonucleotide therapeutic** ~~that receive regulatory approval~~ . Because we are developing oligonucleotides, which are considered a relatively new class of drugs, there is increased risk that the outcome of our clinical trials will not be sufficient to obtain regulatory approval. The FDA and comparable ex- U. S. regulatory agencies have relatively limited experience with **RNA medicines (also known as** oligonucleotides **)** , which may increase the complexity, uncertainty and length of the regulatory review process for our product candidates. To date, the FDA has approved ~~15~~ **17** oligonucleotides for **commercial use** ~~marketing and commercialization~~ . Even though the FDA issued in December 2021 two draft guidance documents relating to IND submissions for individualized antisense oligonucleotide drugs for severely debilitating or life- threatening genetic diseases, one with clinical focus, the other with chemistry manufacturing and controls focus, and in June 2022 a draft guidance on clinical pharmacology considerations for the development of oligonucleotide therapeutics, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to overall development considerations for oligonucleotide drugs. The general lack of policies, practices or guidelines specific to oligonucleotides may hinder or slow review by the FDA or other foreign homologues of any regulatory filings that we may submit. Moreover, the FDA or other foreign homologues may respond to these submissions by defining requirements we may not have anticipated. Addressing such requirements could lead to significant delays in the development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs. As a result of the foregoing factors, we may never receive regulatory approval to market and commercialize any product candidate. Even if we obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may be required to perform additional or unanticipated clinical trials to obtain regulatory approval or be subject to additional post-marketing studies or other requirements to maintain such approval. As a result, we may never succeed in developing a marketable product, we may not become profitable and the value of our ordinary shares could decline. Our preclinical studies and clinical trials may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business ~~will~~ **may** be materially harmed **. We have a robust and diverse pipeline of first- or best- in-class RNA medicines using our RNA editing, splicing, antisense silencing and RNA interference modalities. Our lead programs aim to address both rare and prevalent diseases, including AATD, obesity, DMD and HD** . However, we currently have no products on the market. We have invested a significant portion of our efforts and financial resources in the identification and preclinical and clinical development of our oligonucleotides, the development of **our RNA medicines platform,** PRISM, including our ~~ADAR~~ **RNA** editing capability, and our novel ~~PN backbone~~ chemistry modifications, and the continued growth of our manufacturing capabilities. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development, regulatory approvals, and eventual commercialization of our product candidates. Our success will depend on several factors, including the following: • successfully completing preclinical studies and clinical trials; • successfully conducting process development and manufacturing campaigns in accordance with cGMP; • receiving regulatory approvals from applicable regulatory authorities to market our product candidates and, to the extent necessary, our companion diagnostic tests; • establishing commercial manufacturing capabilities or making arrangements with third party CMOs; • obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates; • the degree to which we are successful in our current collaborations, and any additional collaborations we may establish; • launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; • acceptance of the products, if and when approved, by patients, the medical community and third-party payors; • effectively competing with other therapies; • continuing to maintain an acceptable safety and efficacy profile of the products following regulatory approval; and • appropriately addressing the post- marketing requirements and / or commitments made upon regulatory approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. We may not be able to conduct clinical trials successfully due to various process- related factors that could negatively impact our business plans. The successful initiation and completion of any of our clinical trials, within timeframes consistent with our business plans, is dependent on various factors, which include, but are not limited to, our ability to: • retain and recruit employees, contractors or consultants with the required level of knowledge and experience; • retain and recruit in a timely manner a sufficient number of patients necessary to conduct a clinical trial, which is a function of many factors, including the ~~impact of the COVID- 19 global pandemic, the~~ proximity of participants to clinical sites, the size of the relevant population,

the eligibility criteria for the trial, possible adverse effects from treatments, the existence of competing clinical trials, the involvement of patient advocacy groups, the availability of new or alternative treatments, lack of efficacy, personnel issues and ease of participation in our ~~clinical trials; • manage the impact of the COVID- 19 pandemic on our early- stage discovery efforts and~~ clinical trials; • open study sites, and enroll, treat, and monitor patients due to local restrictions implemented in response to **local** ~~the COVID- 19~~ or ~~other~~ global health ~~pandemics~~ **issues** ; • develop companion diagnostic tests for use with certain of our product candidates or identify partners with such expertise; • manufacture and maintain a sufficient amount of clinical material, internally or through third parties; • ensure adherence to trial designs and protocols agreed upon and approved by regulatory authorities and applicable regulatory and legal guidelines; • apply the appropriate pharmacovigilance measures in case of adverse effects emerging during a clinical trial; • execute clinical trial designs and protocols approved by regulatory authorities without deficiencies; • timely and effectively contract with (under reasonable terms), manage and work with investigators, institutions, hospitals and ~~the~~ contract research organizations (" CROs ") involved in the clinical trial; • negotiate contracts and other related documents with clinical trial parties and ~~institutional review boards (" IRBs ")~~, CRO agreements and site agreements, which can be subject to extensive negotiations that could cause significant delays in the clinical trial process, with terms possibly varying significantly among different trial sites and CROs and possibly subjecting us to various risks; and • conduct clinical trials in a cost- effective manner, including management of foreign currency risk in clinical trials conducted in foreign jurisdictions and cost increases due to unforeseen or unexpected complications such as enrollment delays, or needing to outsource certain functions during the clinical trial. If we are not able to manage the clinical trial process successfully, our business plans could be delayed or be rendered unfeasible for us to execute within our planned or required time frames, or at all. If we cannot successfully manufacture our product candidates for our research and development and preclinical activities, or manufacture sufficient amounts of our product candidates to meet our clinical requirements and timelines, our business may be materially harmed. In order to develop our product candidates, apply for regulatory approvals and commercialize our product candidates, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. In September 2016, we entered into a lease for a multi- use facility of approximately 90, 000 square feet in Lexington, Massachusetts to provide internal cGMP manufacturing capabilities and increase control and visibility of our drug substance supply chain, and we began cGMP manufacturing in this facility at the beginning of 2018. This facility supplements our existing Cambridge, Massachusetts laboratory and office space headquarters, enhances our ability to secure drug substance for current and future development activities and may provide commercial- scale manufacturing capabilities. However, while we have established and continue to enhance our internal cGMP manufacturing capabilities, we have limited experience manufacturing drug substance on a commercial scale, and we will incur significant costs to develop this expertise internally. In addition to the oligonucleotides that we manufacture internally, we may utilize CMOs to manufacture the oligonucleotides required for our preclinical studies and clinical trials. There are a limited number of manufacturers that supply oligonucleotides. There are risks inherent in pharmaceutical manufacturing that could affect our ability or the ability of our CMOs to meet our delivery time requirements or provide adequate amounts of material to meet our clinical trial demands on our projected timelines. Included in these risks are potential synthesis and purification failures and / or contamination during the manufacturing process, as well as other issues with our facility or the CMOs' facilities and ability to comply with the applicable manufacturing requirements and quality standards, which could result in unusable product and cause delays in our manufacturing timelines and ultimately delay our clinical trials, as well as result in additional expense to us. To manufacture our oligonucleotides, we rely on third parties to supply the required raw materials. We will likely need to secure alternative suppliers for these raw materials, and such alternative suppliers are limited and may not be readily available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner. For example, we source certain materials used in the manufacture of our products from China and other countries outside of the United States **,** ~~; the coronavirus outbreak or other similar global disruptions has made access to our existing supply chain difficult~~ and ~~further~~ supply chain disruptions could impact our business. Additionally, our cost of goods development is at an early stage. The actual cost to manufacture and process our product candidates could be greater than we expect and could materially and adversely affect the commercial viability of our product candidates. The process of manufacturing oligonucleotides is complex and we may encounter difficulties in production, particularly with respect to process development or scaling- up of our manufacturing capabilities. The process of manufacturing oligonucleotides is complex, highly- regulated and subject to multiple risks. The complex processes associated with the manufacture of our product candidates expose us to various manufacturing challenges and risks, which may include delays in manufacturing adequate supply of our product candidates, limits on our ability to increase manufacturing capacity, and the potential for product failure and product variation in quality that may interfere with preclinical studies and clinical trials, along with additional costs. We also may make changes to our manufacturing process at various points during development, and even after commercialization, for various reasons, such as optimizing costs, achieving scale, decreasing processing time, increasing manufacturing success rate, or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of current or future clinical trials, or the performance of the product, once commercialized. In some circumstances, changes in the manufacturing process may require us to perform ex vivo comparability studies, and / or conduct animal studies, and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical trials or at earlier portions of a trial to the product used in later clinical trials or later portions of the trial. We may also make further changes to our manufacturing process before or after commercialization, and such changes may require us to show the comparability of the resulting product to the product produced via earlier manufacturing processes and supplied in clinical studies. We may be required to collect additional preclinical and / or clinical data from any modified process prior to obtaining marketing approval for the product candidate produced with such modified process. If preclinical and / or clinical data are not ultimately comparable to those seen in the earlier trials, we may be

required to make further changes to our process and / or undertake additional clinical testing, either of which could significantly delay the clinical development or commercialization of the associated product candidate. We ~~have~~ **are** a **clinical** ~~robust and diverse pipeline of PN~~ ~~modified, stereopure~~ **stage biotechnology company focused on unlocking the broad potential of RNA medicines (also known as** oligonucleotides **)** , ~~including programs using our~~ **or those targeting ribonucleic acid (RNA), to transform human health. Our RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Our toolkit of RNA- targeting modalities includes RNA** editing, splicing, ~~and~~ **antisense** silencing ~~modalities~~ **and RNA interference, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology** . Our lead ~~clinical~~ programs are ~~focused~~ in ~~,~~ **rare** and **prevalent** ~~aim to address, muscle~~ diseases ~~( , including AATD, obesity,~~ DMD ~~– splicing)~~ , ~~hepatic diseases (AATD – editing),~~ and ~~CNS diseases (~~HD ~~, ALS and FTD – silencing)~~ . Although we continue to build on our experience in manufacturing oligonucleotides, we have limited experience as a company manufacturing product candidates for commercial supply. We may never be successful in manufacturing product candidates in sufficient quantities or with sufficient quality for commercial use. Our manufacturing capabilities could be affected by cost- overruns, unexpected delays, equipment failures, labor shortages, operator error, natural disasters, unavailability of qualified personnel, difficulties with logistics and shipping, problems regarding yields or stability of product, contamination or other quality control issues, power failures, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business. Furthermore, compliance with cGMP requirements and other quality issues may arise during our internal efforts to scale- up manufacturing, and with our current or any future CMOs. If contaminants are discovered in our supply of our product candidates or in our manufacturing facilities or those of our CMOs, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability failures or other issues relating to the manufacture of our product candidates will not occur in the future. Additionally, we and our CMOs may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If we or our CMOs were to encounter any of these difficulties, our ability to provide our product candidate to patients in clinical trials, or to provide product for treatment of patients once approved, would be jeopardized. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any product candidates we develop may fail in preclinical or clinical development or be delayed to a point where they do not become commercially viable. Before obtaining regulatory approval for the commercial distribution of any of our product candidates, we must conduct, at our own expense, extensive preclinical studies and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Preclinical and clinical testing ~~are~~ **is** expensive, difficult to design and implement, can take many years to complete, ~~are~~ **is** uncertain as to outcome, and the historical failure rate for drugs in preclinical and clinical development is high. For example, we depend on the availability of non- human primates to conduct certain preclinical studies. Over the past several years there has been **a** ~~an increasing~~ global shortage of non- human primates available for drug development that has matured into an acute global supply chain issue. The supply of these non- human primates ~~is currently~~ **has been** constrained due to factors such as their limited worldwide availability, domestic regulatory restrictions and trade relations. If we are unable to obtain access to a sufficient supply of these non- human primates in a timely manner or at all, our timelines and our ability to complete preclinical testing and submit **IND /** CTA **or equivalent foreign** applications may be adversely affected. We, the FDA or comparable foreign regulatory authorities or an IRB, or similar foreign review board or ethics committee, may suspend clinical trials of a product candidate at any time for various reasons, including if we or they believe the healthy volunteer subjects or patients participating in such trials are being exposed to unacceptable health risks. Among other reasons, unacceptable side effects or other more serious adverse events of a product candidate in healthy volunteer subjects or patients in a clinical trial could result in the FDA or comparable foreign regulatory authorities suspending or terminating the trial and refusing to approve a particular product candidate for any or all indications of use. Clinical trials also require the review, oversight and approval of IRBs or ethics committees, which review the clinical protocols and informed consent form for investigations that will be conducted at their institutions in order to protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB approval can prevent or delay the initiation and completion of clinical trials at particular sites. Furthermore, failure to provide information to the IRB and relevant regulatory authorities, as required throughout the study, such as emergent safety reports and annual updates, may result in suspension of the approval of the trial. Our product candidates may encounter problems during clinical trials that will cause us or regulatory authorities to delay, suspend or terminate these trials, or that will delay or confound the analysis of data from these trials. If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected or any of our other product candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected product candidate and for other product candidates we are developing. The development of one or more of our product candidates can fail at any stage of testing. We may experience numerous unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or

prevent regulatory approval or our ability to commercialize our product candidates, including: • our preclinical studies or clinical trials may produce negative or inconclusive results, including results that may not meet the level of significance or clinical benefit required by the FDA or other regulators, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may abandon projects that we had expected to be promising; • delays in filing ~~clinical trial applications~~ **INDs / CTAs** or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced; • conditions imposed on us by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials; • divergent views between FDA and other homologue regulatory authorities as to the objectives and / or design of the clinical trials required in support of marketing registration; • problems in obtaining or maintaining IRB approval of trials; • delays in enrolling patients or volunteers into clinical trials, and variability in the number and types of patients eligible for clinical trials; • delays in developing and receiving regulatory approval for companion diagnostic tests, to the extent such tests are needed, to identify patients for our clinical trials; • high drop- out rates for patients in clinical trials and substantial missing data; • an inability to open study sites, or enroll, treat, and monitor patients due to local restrictions implemented in response to **local or global health epidemics, including emerging or future variants of** COVID- 19 ~~(emerging or future variants of COVID- 19) or other global health pandemics~~ ; • negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours; • results from future clinical trials may not confirm positive results, if any, from earlier preclinical studies and clinical trials; • inability to consistently manufacture, inadequate supply, or unacceptable quality of product candidate materials or other materials necessary for the conduct of our clinical trials; • greater than anticipated clinical trial costs; • serious and unexpected side effects that may or may not be related to the product candidate being tested that are experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; • poor or disappointing effectiveness of our product candidates during clinical trials; • unfavorable outcome of FDA or other regulatory agency inspection and review of a manufacturing or clinical trial site or other records relating to the clinical investigation; • failure of our third- party contractors, investigators, or collaboration partners to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all; • governmental or regulatory delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around manufacturing, preclinical, or clinical testing generally or with respect to our product candidates class, in particular; or • varying interpretations of data by the FDA and similar foreign regulatory agencies. If we do not successfully conduct clinical development, we will not be able to market and sell products derived from our product candidates and to generate product revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before we can submit an application for regulatory approval to the FDA or foreign regulatory agencies. If the development of any of our product candidates fails or is delayed to a point where such product candidate is no longer commercially viable, our business may be materially harmed. Results of preclinical studies and early clinical trials may not be predictive of results of ~~future~~ **subsequent** clinical trials. The results from preclinical studies or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent subjects or in subsequent clinical trials of that product candidate or any other product candidate. The design of a clinical trial can determine whether its results will support approval of a product candidate and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Product candidates that seemingly perform satisfactorily in preclinical studies may nonetheless fail to reach late development stages or obtain regulatory approval for marketing. For example, our preclinical studies for ~~suvodirsen~~ **WVE- 004 for C9orf72- associated amyotrophic lateral sclerosis and frontotemporal dementia (" C9- ALS / FTD ")** yielded positive results. However, in ~~December 2019~~ **May 2023** , the ~~interim analysis~~ **topline results** of the Phase ~~1 open~~ **1b / 2a study of WVE** - **004** ~~label extension (OLE) study of suvodirsen~~ for patients with ~~DMD~~ **C9- ALS / FTD** showed no **trends in clinical benefit and reductions in poly (GP) were not correlated with** ~~change~~ **changes** ~~from baseline~~ in ~~dystrophin expression~~ **functional outcome** and resulted in our discontinuation of the ~~suvodirsen~~ **WVE- 004** program. There is a high failure rate for drugs proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could negatively affect our business and operating results. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including **local or** ~~the COVID- 19~~ global **health issues** ~~pandemic or emerging or future variants of COVID- 19~~ , the size of the patient population, the age and condition of the patients, the stage and severity of disease, the nature and requirements of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. Delays or difficulties in patient enrollment or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments, can result in increased costs, longer development times or termination of a clinical trial. In addition, our success may depend, in part, on our ability to identify patients who qualify for our clinical trials, or are likely to benefit from any medicines that we may develop, which will require those potential patients to undergo a screening assay, which we also refer to as a companion diagnostic test, for the presence or absence of a particular genetic sequence. For example, in HD, we are conducting a clinical trial for WVE- 003, which targets a SNP associated with the mutant allele of the HTT gene. Approximately 40 % of the HD patient population carry this SNP. We have developed a novel screening assay that is intended to identify whether a patient has the particular SNP that our product candidate is targeting, and **we have** partnered with a third party for testing in future trials. If we, or any third parties that we engage to assist us are unable to successfully identify patients with the appropriate SNP that we are targeting, the percentage of

patients with the SNP we are targeting is lower than expected, or we experience delays in testing, we may not realize the full commercial potential of any product candidates we develop **. Congress also recently amended the FDCA to require sponsors of a Phase 3 clinical trial, or other " pivotal study " of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must describe appropriate diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Although none of our product candidates has reached Phase 3 of clinical development, we must submit a diversity action plan to the FDA by the time we submit a Phase 3 trial, or pivotal study, protocol to the agency for review, unless we are able to obtain a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect the planning and timing of any future Phase 3 trial for our product candidates or what specific information the FDA will expect in such plans. However, initiation of such trials may be delayed if the FDA objects to our proposed diversity action plans for any future Phase 3 trial for our product candidates, and we may experience difficulties recruiting a diverse population of patients in attempting to fulfill the requirements of any approved diversity action plan** . If we are unable to successfully develop or obtain regulatory approval for companion diagnostic tests for our product candidates, or experience significant delays in doing so, our clinical trials may be delayed and our business could be materially harmed. The development programs for some of our product candidates contemplate the development of companion diagnostic tests, which are assays or tests to identify an appropriate patient population. The success of certain of our product candidates will depend on several factors, including the successful development of, and ability to obtain regulatory approval for, companion diagnostic tests that will be used to screen and identify the right patients for our product candidates. Our goal is to develop and commercialize disease- modifying medicines for genetically defined diseases with a high degree of unmet medical need, and to become a fully integrated ~~genetic~~ **RNA** medicines company. The target patient populations for several of our product candidates are relatively small, and it will be difficult to successfully identify the appropriate patients for whom our product candidates are being designed without performant, fit- for- purpose, accessible, relatively inexpensive, and easy- to- use companion diagnostic tests. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices, often in vitro devices, and require separate regulatory authorization prior to commercialization. We are not a medical device company, and we have limited experience developing medical devices. A more detailed description of the FDA approval process for companion diagnostic tests is included under " Business – Government Regulation – In Vitro Diagnostic Tests for Biomarkers. " Given our limited experience in developing and commercializing companion diagnostic tests, we may seek to collaborate with third parties to assist us in the design, manufacture, regulatory authorization and commercialization of the companion diagnostic tests for some of our product candidates. In November 2019, we entered into a collaboration with Asuragen ~~, Inc. (" Asuragen ")~~ for the development and commercialization of companion diagnostics for our allele- selective product candidate in HD. We, Asuragen and other potential collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostic tests, including issues relating to sensitivity / specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory authorization of the relevant companion diagnostic tests could delay or prevent approval of our product candidates. If we, Asuragen or any other third parties that we engage to assist us, are unable to successfully develop, validate, and commercialize companion diagnostic tests for our drug candidates, or experience delays in doing so, our clinical trials and our business could be materially harmed. We may be unable to obtain regulatory approval in the United States or foreign jurisdictions and, as a result, be unable to commercialize our product candidates and our ability to generate revenue will be materially impaired. Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, quality, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical studies and clinical trials, and an extensive regulatory approval process are required to be successfully completed in the United States and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to a continuously evolving regulatory environment and unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them. The time required to obtain FDA and other approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating companies such as ours are not always applied predictably or uniformly and can change. Any analysis we perform of data from chemistry, manufacturing and controls, preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. Any delay or failure in obtaining required approvals could adversely affect our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy (" REMS "), as a condition of approval, which may impose further requirements or restrictions on the distribution or safe use of an approved drug, such as limiting prescribing rights to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients as specially defined by the indication statement or who meet certain safe- use criteria, and requiring treated patients to enroll in a registry, among other requirements. These limitations and restrictions may limit the size of the market for the product and affect reimbursement by third- party payors. We are also subject to numerous foreign regulatory requirements

governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and payment. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above, as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Approval by the FDA does not ensure approval by comparable regulatory authorities outside of the United States and vice versa. If we are granted orphan drug designations in the United States for any of our product candidates, there can be no guarantee that we will maintain orphan status for these product candidates or receive approval for any product candidate with an orphan drug designation. Subject to receiving approval from the FDA of an NDA or Biologics License Application (" BLA "), products granted orphan drug designation are provided with seven years of orphan marketing exclusivity in the United States, meaning the FDA generally will not approve applications for other product candidates for the same orphan indication that contain the same active ingredient. We are not guaranteed to maintain or receive orphan designation for our current or future product candidates, and if our product candidates that were granted orphan designation were to lose their status as an orphan drug or the orphan marketing exclusivity provided to it in the United States, our business and results of operations could be materially adversely affected. While orphan status for any of our products, if granted or maintained, would provide market exclusivity in the United States for the time periods specified above, we would not be able to exclude other companies from manufacturing and / or selling products using the same active ingredient for the same indication beyond the exclusivity period applicable to our product on the sole basis of orphan drug status. In addition, orphan exclusivity does not block the approval of a different drug or biologic for the same rare disease or condition, nor does it block the approval of the same drug or biologic for different conditions. Even if we are the first to obtain approval of an orphan product candidate and are granted exclusivity in the United States, there are circumstances under which a later competitor product may be approved for the same indication during the period of marketing exclusivity, such as if the later product is shown to be clinically superior to our product or if we are not able to provide a sufficient quantity of the orphan drug. Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight. If we **or our collaborators or contractors** fail to comply with continuing U. S. and foreign requirements, our approvals, if obtained, could be limited or withdrawn, we could be subject to other penalties, and our business would be seriously harmed. Following any initial regulatory approval of any drugs we may develop, we will also be subject to continuing regulatory oversight, including the review of adverse drug experiences and safety data that are reported after our drug products are made commercially available. This would include results from any post- marketing studies or surveillance to monitor the safety and efficacy of the drug product required as a condition of approval or agreed to by us. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved uses for which the product may be marketed. Other ongoing regulatory requirements include, among other things, submissions of safety and other post- marketing information and reports, registration and listing, as well as continued maintenance of our marketing application, compliance with cGMP requirements and quality oversight, compliance with post- marketing commitments, and compliance with GCP for any clinical trials that we conduct post- approval. Failure to comply with these requirements could result in warning or untitled letters, criminal or civil penalties, recalls, or product withdrawals. In addition, we are conducting our clinical trials and we intend to seek approval to market our product candidates in jurisdictions outside of the United States, and therefore will be subject to, and must comply with, regulatory requirements in those jurisdictions. The FDA has significant post- market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials for a variety of reasons. The FDA also has the authority to require a REMS plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. We, our CMOs, and the manufacturing facilities we use to make our product candidates will also be subject to ongoing assessment of product quality, compliance with cGMP, and periodic inspection by the FDA and potentially other regulatory agencies. We or our CMOs may not be able to comply with applicable cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our CMOs, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. We may not have the ability or capacity to manufacture material at a broader commercial scale in the future. We and our CMOs currently manufacture a limited supply of clinical trial materials. Reliance on CMOs entails risks to which we would not be subject if we manufactured all of our material ourselves, including reliance on the CMO for regulatory compliance. Our product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. If we or our collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the United States or foreign jurisdictions in which we may seek to market our products, we or they may be subject to, among other things, fines, warning letters, holds on clinical trials, refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, refusal to permit the import or export of products, operating restrictions, injunction, consent decree, civil penalties and criminal prosecution. Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which will prevent us from becoming profitable. Our product candidates are based upon new discoveries, technologies and therapeutic approaches. Key participants in pharmaceutical marketplaces, such as physicians, third- party payors and consumers, may not adopt a product intended to improve therapeutic results that is based on the technology employed by oligonucleotides. As a result, it may be more difficult for us to convince the medical community and third- party payors to accept and use our product, or to provide favorable reimbursement. Other factors that we believe will materially affect market acceptance of our product candidates include: • the timing of our receipt of any regulatory approvals, the terms of any approvals and the countries in which approvals are obtained; • the ability to consistently manufacture our products within acceptable quality standards; • the safety

and efficacy of our product candidates, as demonstrated in clinical trials and as compared with alternative treatments, if any; • the incidence, seriousness and severity of any side effects; • the relative convenience and ease of administration of our product candidates; • the willingness of patients to accept potentially new routes of administration and their risk tolerance as it relates to potentially serious side effects; • the success of our physician education programs; • the availability of government and third-party payer coverage and adequate reimbursement; • the pricing of our products, particularly as compared to alternative treatments; and • the availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat and the relative risks, benefits and costs of those treatments. In addition, our estimates regarding the potential market size may be materially different from what we currently expect at the time we commence commercialization, which could result in significant changes in our business plan and may significantly harm our results of operations and financial condition. The pharmaceutical industry is intensely competitive. If we are unable to compete effectively with existing drugs, new treatment methods and new technologies, we may be unable to commercialize successfully any drugs that we develop. The pharmaceutical industry is intensely competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs for the same diseases that we are targeting or expect to target. Many of our competitors have: • much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products; • more extensive experience in designing and conducting preclinical studies and clinical trials, obtaining regulatory approvals, and manufacturing, marketing and selling pharmaceutical products; • product candidates that are based on previously tested or accepted technologies; • products that have been approved or are in late stages of development; and • collaborative arrangements in our target markets with leading companies and research institutions. We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. We also expect to face competition from new drugs that enter the market. We believe a significant number of drugs are currently under development, and may become commercially available in the future, for the treatment of conditions that our current or future product candidates are or may be designed to treat. These drugs may be more effective, safer, less expensive, or marketed and sold more effectively, than any products we develop. Our competitors may develop or commercialize products with significant advantages over any products we are able to develop and commercialize based on many different factors, including: • the safety and effectiveness of our products relative to alternative therapies, if any; • the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration; • the timing and scope of regulatory approvals for these products; • the availability and cost of manufacturing, marketing and sales capabilities; • price; • more extensive coverage and higher levels of reimbursement; and • patent position. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute on our business plan. If we or our collaborators, manufacturers, service providers or other third parties fail to comply with applicable healthcare laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our products and may harm our reputation. We are currently, or may in the future, be subject to federal, state, local, and comparable foreign healthcare laws and regulations relating to areas such as fraud and abuse and patients' rights. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our products for which we obtain marketing approval. These laws and regulations include: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for a healthcare item or service, or the purchasing, recommending, or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid; • the U. S. federal false claims and civil monetary penalties laws, including the False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government- funded programs such as Medicare or Medicaid that are false or fraudulent, or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government; • ~~the U. S. federal Health Insurance Portability and Accountability Act (" HIPAA ")~~, which, among other things, criminalizes a wide array of conduct involving public and private healthcare benefits, creates new civil enforcement mechanisms and increases civil and criminal penalties for healthcare fraud; • HIPAA **,** as amended by the ~~Health Information Technology for Economic and Clinical Health (" HITECH ")~~ Act, and its implementing regulations, which strengthen and expand requirements relating to the privacy, security, and transmission of individually identifiable health information; and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information; • the U. S. federal Physician Payments Sunshine Act, which requires certain manufacturers of medical devices, biological products, medical supplies, and drugs for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program, with specific exceptions, to report annually to ~~the Centers for Medicare and Medicaid Services (" CMS ")~~ all transfers of value ~~, including consulting fees, travel reimbursements, research grants, and other payments or gifts with values over $ 10~~ made to physicians, certain advanced non- physician ~~health~~ **healthcare** ~~care~~ practitioners, or teaching hospitals and requires applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. Disclosure of such information is made by CMS on a publicly available website; and • state and foreign laws comparable to each of the above federal laws, such as, for example: state anti- kickback and false claims laws applicable to commercial insurers and other non- federal payors; state laws that require pharmaceutical manufacturers to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the

federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information, some which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, criminal prosecution, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in federal healthcare programs including Medicare and Medicaid, the imposition of a corporate integrity agreement with the Office of Inspector General **for DHHS** ~~of the Department of Health and Human Services~~ , disgorgement, individual imprisonment, contractual damages, reputational harm, and diminished profits and future earnings, any of which could adversely affect our financial results and adversely affect our ability to operate our business. We intend to develop and implement a comprehensive corporate compliance program prior to the commercialization of our product candidates. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses, could divert our management' s attention from the operation of our business, and could harm our reputation, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources. **Furthermore, if the FDA or a comparable foreign regulatory authority approves any of our drug candidates, activities such as the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and record keeping for the products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as continued compliance with cGMP. The FDA or a comparable foreign regulatory authority may also impose requirements for costly post- marketing nonclinical studies or clinical trials (often called " Phase 4 trials ") and post- marketing surveillance to monitor the safety or efficacy of the product.** If **we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, production issues with the facility where the product is manufactured or processed, such as product contamination or significant non- compliance with applicable cGMP requirements, a regulator may impose restrictions on that product, the manufacturing facility or us. If we or our collaborators or third- party service providers, including our CMOs, fail to comply fully with applicable regulations, then we may be required to initiate a recall or withdrawal of our products. If previously unknown problems with one of our products, if approved, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes are discovered, or if** we or our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others: • adverse regulatory inspection findings; • warning and / or untitled letters; • voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals; • restrictions on, or prohibitions against, marketing our products; • restrictions on, or prohibitions against, importation or exportation **of our products; • restrictions on the labeling, use or distribution** of our products; • suspension of review or refusal to approve pending applications or supplements to approved applications; • exclusion from participation in government- funded healthcare programs; • exclusion from eligibility for the award of government contracts for our products; • suspension or withdrawal of product approvals; • product seizures; • injunctions; • consent decrees; and • civil and criminal penalties, up to and including criminal prosecution resulting in fines, exclusion from healthcare reimbursement programs and imprisonment. Moreover, federal, state or foreign laws or regulations are subject to change, and while we, our collaborators, manufacturers and / or service providers currently may be compliant, that could change due to changes in interpretation, prevailing industry standards or other reasons. Any drugs we develop may become subject to unfavorable pricing regulations, third- party reimbursement practices or healthcare reform initiatives, thereby harming our business. Because our product candidates represent new approaches to the treatment of genetic- based diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. 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 product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. We are monitoring these regulations as several of our programs move into later stages of development; however, many of our programs are currently in the earlier stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that could delay our commercial launch of the product and negatively impact any potential revenues we may be able to generate from the sale of the product in that country and potentially in other countries due to reference pricing **or other measures to reduce drug prices** . Our ability to commercialize any products successfully will also depend in part on the extent to which coverage and adequate reimbursement / payment for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if we succeed in bringing one or more products to the market, these products may not be considered medically necessary and / or cost- effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. At this time, we are unable to determine their cost effectiveness or the likely level or method of reimbursement for our product candidates. Increasingly, third- party payors, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts paid for

pharmaceutical products. If the price we are able to charge for any products we develop, or the payments provided for such products, is inadequate in light of our development and other costs, our return on investment could be adversely affected. We currently expect that any drugs we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U. S. law, certain drugs that are not usually self- administered (such as most injectable drugs) may be eligible for coverage under the Medicare Part B program if: • they are incident to a physician' s services; • they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice; and • they have been approved by the FDA and meet other requirements of the statute. There may be significant delays in obtaining coverage for newly- approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third- party payors to pay all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and payment is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate payment is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Moreover, eligibility for coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement may be based on payments allowed for lower- cost drugs that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. However, no uniform policy requirement for coverage and reimbursement for drug products exists among third- party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time- consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Our inability to promptly obtain coverage and adequate reimbursement rates from both government- funded and private payors for new drugs that we develop and for which we obtain regulatory approval could adversely affect our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition. **Further,** ~~We believe that the~~ **there have been, and may continue to be, legislative and regulatory proposals at the U. S. federal and state levels and in foreign jurisdictions directed at broadening the availability and containing or lowering the cost of healthcare. The continuing** efforts of **the** ~~governments~~ **government, insurance companies, managed care organizations** and **other** third- party payors to contain or reduce ~~the cost~~ **costs** of healthcare **may adversely** ~~and legislative and regulatory proposals to broaden the availability of healthcare will continue to~~ affect ~~the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the United States and other major healthcare markets have been proposed and / or~~ **our ability to set prices for our products** ~~adopted in recent years, and such efforts have expanded substantially in recent years. These developments have included prescription drug benefit legislation~~ that ~~was enacted in 2003 and took effect in January 2006~~ **would allow us to achieve or sustain profitability. In addition** , **governments may impose price controls on any of our products** ~~healthcare reform legislation enacted by certain states, and major healthcare reform legislation~~ that **obtain marketing approval** ~~was passed by Congress and enacted into law in the United States in 2010. These developments could~~ , **which may adversely** ~~directly or indirectly,~~ affect our **future profitability** ~~ability to sell our products, if approved, at a favorable price~~ . **The Inflation Reduction** ~~In particular, in March 2010, the Patient Protection and Affordable Care~~ Act **of 2022** ( ~~the~~ " ~~ACA~~ **IRA** ") was signed into law ~~. This~~ **in August 2022 (see above " Government** ~~legislation~~ **Regulation — changed the system of healthcare** **Healthcare Reform "). In addition** ~~insurance and benefits and was intended to broaden access to healthcare coverage~~ , **Executive Order 14087** ~~enhance remedies against fraud and abuse~~ , **issued October 2022** ~~add transparency requirements for the healthcare and health insurance industries~~ , ~~impose taxes~~ **called for CMS to prepare** and ~~fees~~ **submit a report to the White House** on **potential payment** ~~the healthcare industry, impose health policy reforms,~~ and **delivery modes** ~~control costs. This law also contains provisions~~ that would ~~affect companies in~~ **complement to IRA, lower drug costs, and promote access to innovative drugs. In February 2023, CMS published its report which described** ~~the~~ **three potential models focusing on affordability, accessibility and feasibility of implementation for further testing by the CMS Innovation Center. As of February 2024, the CMS Innovation Center continues to test the proposed models and has started to roll out plans for access model testing of certain product types (e. g., cell and gene therapies) by states and manufacturers. Additional state and federal healthcare reform measures are expected to be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for certain biopharmaceutical products or additional pricing pressures. In some foreign countries, particularly the member states of the European Union, the pricing of prescription** ~~pharmaceutical~~ **pharmaceuticals** ~~industry~~ **is subject to governmental control. In these countries, pricing negotiations with governmental authorities can be a long and expensive process after the receipt of marketing approval for a drug candidate. In addition, there can be considerable pressure by governments** and other **stakeholders on** ~~healthcare related industries by imposing additional costs and changes to business practices~~ --- **prices** . ~~Since its enactment, there have been judicial~~ and ~~Congressional challenges to certain aspects of the ACA. The uncertainty around the future of the ACA, and in particular the impact to~~ reimbursement levels, **including** ~~may lead to uncertainty or delay in the purchasing decisions of our~~

~~customers, which may in turn negatively impact our product sales. We continue to evaluate the effect that the ACA has~~ **as part of cost containment measures** ~~or any potential changes to the ACA could have on our business~~. **Political, economic** ~~Additional federal and state legislative~~ and regulatory developments ~~are likely~~ **may further complicate pricing negotiations** , and ~~we expect ongoing initiatives in the United~~ **pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member** ~~States~~ **states and parallel distribution, or arbitrage between low- priced and high- priced member states, can further reduce prices. In some countries, we may be required** to ~~increase~~ **conduct additional clinical trials that compare the cost- effectiveness of our drug candidates to other available therapies in order to obtain reimbursement or pricing approval. Publication of discounts by third- party payors or authorities may lead to further** pressure on **prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to successfully commercialize and achieve or sustain profitability for sales of any of our** drug ~~pricing and reimbursement. Such reforms could have an adverse effect on anticipated revenues from product~~ candidates that **are** ~~we may successfully develop and for which we may obtain regulatory approval~~ **approved for marketing in that country** and ~~may~~ **our business could be adversely** ~~affect~~ **affected** ~~our overall financial condition and ability to develop product candidates~~. Changes in laws and regulations affecting the healthcare industry could adversely affect our business. All aspects of our business, including research and development, manufacturing, marketing, pricing, sales, litigation, and intellectual property rights, are subject to extensive legislation and regulation. Changes in applicable U. S. federal and state laws and agency regulation, as well as foreign laws and regulations, could have a materially negative impact on our business. In the United States and in some other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates or any potential future product candidates of ours, restrict or regulate post- approval activities, or affect our ability to profitably sell any product candidates for which we obtain marketing approval. Increased scrutiny by the U. S. Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. Congress also must reauthorize the FDA' s user fee programs every five years and often makes changes to those programs in addition to policy or procedural changes that may be negotiated between the FDA and industry stakeholders as part of this periodic reauthorization process. Congress most recently reauthorized the user fee programs in September 2022 without any substantive policy changes. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in ~~health~~ **healthcare** ~~care~~ systems with the stated goals of containing ~~health~~ **healthcare** ~~care~~ costs, improving quality and / or expanding access. In the United States, the pharmaceutical industry has been a focus of these efforts and has been significantly affected by major legislative initiatives. ~~In~~ **For example, in** March 2010, Congress passed the ACA, which ~~substantially changed~~ **, among** ~~the~~ **other** ~~way health~~ **things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed** care **plans; imposed mandatory discounts for** ~~is financed by both the government and private insurers, and significantly impacts the U. S. pharmaceutical industry. There remain judicial and Congressional challenges to~~ certain **Medicare Part D beneficiaries** ~~aspects of the ACA, and~~ as a **condition** ~~result certain sections of the ACA have not been fully implemented or~~ **for manufacturers' outpatient drugs coverage under Medicare Part D; and established** ~~effectively repealed. However, following several years of litigation in the federal courts, in June 2021, the U. S. Supreme Court upheld the ACA when it dismissed~~ a ~~legal challenge to~~ **Center for Medicare Innovation at** the ~~law~~ **CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. In addition to the IRA** ' s **drug price negotiation provisions summarized above** ~~constitutionality. Further legislative and regulatory changes under the ACA remain possible~~ , ~~although~~ **Executive Order 14087, issued in October 2022, called for** the ~~new federal administration under President Biden has signaled~~ **CMS Innovation Center to prepare and submit a report to the White House on potential payment and delivery modes** that **would complement to IRA, lower drug costs, and promote access to innovative drugs. In February 2023, CMS published** ~~it~~ **its** ~~plans to build~~ **report which described three potential models focusing** on ~~the ACA~~ **affordability, accessibility** and **feasibility** ~~expand the number~~ of **implementation** ~~people who are eligible~~ for ~~health insurance subsidies under it~~ **further testing by the CMS Innovation Center** . ~~It~~ **As of February 2024, the CMS Innovation Center' s testing of the proposed models** is **still** ~~unknown what form any such changes or any law would take, and how or whether it may affect the pharmaceutical industry as a whole or our business~~ in **progress** ~~the future~~ . We expect that **future** changes or additions to the ACA, the Medicare and Medicaid programs, and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry in the United States. ~~The uncertainty around the future of the ACA, and in particular the impact to reimbursement levels, may lead to uncertainty or delay in the purchasing decisions of our customers, which may in turn negatively impact our product sales. If there are not adequate reimbursement levels, our business and results of operations could be adversely affected. 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 up to 2 % per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and was extended by the Consolidated Appropriations Act for 2023, and will remain in effect through 2032 unless additional Congressional action is taken. In addition, the Drug Supply Chain Security Act enacted in 2013 imposed obligations on manufacturers of pharmaceutical products related to product tracking and tracing, and in February 2022, FDA released proposed regulations to amend the national standards for licensing of wholesale drug distributors by the states; establish new minimum standards for state licensing third- party logistics providers; and create a federal system for licensure for use in the absence of a State program, each of which is mandated by the~~

~~DSCSA. As another example, in December 2019, the Further Consolidated Appropriations Act for 2020 (P. L. 116- 94) was enacted that includes a piece of bipartisan legislation called the CREATES Act. The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic and biosimilar product developers access to samples of brand products. The CREATES Act establishes a private cause of action that permits a generic or biosimilar product developer to sue the brand manufacturer to compel it to furnish the necessary samples on " commercially reasonable, market- based terms. " Whether and how generic and biosimilar product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown. Other legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. We are unsure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or whether such changes will have any impact on our business.~~ Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices considering the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products ~~. For example, state legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U. S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers (PBMs) and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area. At the federal level, DHHS has solicited feedback on various measures intended to lower drug prices and reduce the out of pocket costs of drugs and has implemented others under its existing authority~~ . For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS' s policy change that was effective January 1, 2019. ~~Most recently~~ **In addition** , **the** ~~in August 2022~~ **2021** ~~, President Biden~~ **Consolidated Appropriations Act** signed into ~~the~~ law **on December 27,** ~~the Inflation Reduction Act of 2022~~ **2020 incorporated extensive healthcare** ~~(the " IRA "). Among other things, the IRA has multiple~~ provisions **and amendments to existing laws, including a requirement** that **all manufacturers** ~~may impact the prices~~ of drug products **covered under** ~~that are both sold into the~~ Medicare ~~program and throughout the United States. Starting in 2023, a manufacturer of a drug or biological product covered by Medicare Parts~~ **Part** B **report** ~~or D must pay a rebate to the federal government if~~ the product' s **average sales** price **to CMS beginning** ~~increases faster than the rate of inflation. This calculation is made~~ on ~~a~~ **January 1, 2022, subject to enforcement via civil money penalties. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription** drug ~~product~~ **payment limits. In December 2020, the U. S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate PBMs and other members of the healthcare and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts** by ~~drug product basis and~~ **states in this area. In mid- 2022,** the ~~amount of~~ **FTC also launched sweeping investigations into** the **practices** ~~rebate owed to the federal government is directly dependent on the volume~~ of ~~a drug product~~ **the PBM industry** that **could lead to** ~~is paid for by Medicare Parts B or D. Additionally, starting in payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. Any~~ additional federal ~~or~~ **and** state ~~health~~ **legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. In addition, in the last few years, several states have formed prescription drug affordability boards (" PDABs ") with the authority to implement upper payment limits (" UPLs ") on drugs sold in their respective jurisdictions. There** ~~care~~ **are several pending federal lawsuits challenging the authority of states to impose UPLs, however. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal healthcare** reform measures **will be adopted in the future, any of which** could limit the amounts that ~~third- party payers~~ **federal and state governments** will pay for ~~future health~~ **healthcare** ~~care~~ products and services ~~, and, in turn, could significantly reduce the projected value of certain development projects and reduce our profitability~~ . Risks associated with our operations outside of the United States and developments in international trade by the U. S. and foreign governments could adversely affect our business. We have operations and conduct business outside the United States, and we plan to continue to expand these operations. Therefore, we are subject to risks related to operating in foreign countries, which include unfamiliar foreign laws or regulatory requirements or unexpected changes to those laws or requirements; other laws and regulatory requirements to which our business activities abroad are subject, such as the Foreign Corrupt Practices Act and the U. K. Bribery Act; changes in the political or economic condition of a specific country or region, including Russia' s invasion of Ukraine **, the conflict in the Middle East,** and the potential for a wider European or global conflict; fluctuations in the value of foreign currency versus the U. S. dollar; ~~increasing~~ inflation and interest rate changes ~~,~~ **;** our ability to deploy overseas funds in an efficient manner; tariffs, trade protection measures, import or export licensing requirements, trade embargoes, and sanctions

(including those administered by the Office of Foreign Assets Control of the U. S. Department of the Treasury), and other trade barriers; global instability from an outbreak of pandemic or contagious disease, ~~including the COVID- 19 global pandemic and variants thereof;~~ difficulties in attracting and retaining qualified personnel; and cultural differences in the conduct of business. For example, given developments related to international trade over the past few years, unexpected changes in tariffs could adversely affect our cost of goods sold and / or the foreign sales of our product candidates. **Changes impacting our ability to** ~~Further complicating potential uncertainties caused by conducting~~ --- **conduct** business outside **of** the United States ~~are political movements that are changing decades- old institutions, including, for example, in 2016, the United Kingdom held a referendum in which voters approved an exit from the European Union, commonly referred to as " Brexit. " The withdrawal of the United Kingdom from the European Union took effect on January 31, 2020, the effective date of the withdrawal agreement, with a transition period that ended on December 31, 2020. Since a significant proportion of the regulatory framework in the United Kingdom was, prior to Brexit, derived from European Union directives and regulations, Brexit and the new Trade and Cooperation Agreement between the European Union and the United Kingdom that took provisional effect on January 1, 2021 could materially impact the regulatory regime with respect to the approval of any product candidates in the United Kingdom. Changes impacting our ability to conduct business in the United Kingdom or other European Union countries~~ , or changes to the regulatory regime applicable to our operations in ~~those~~ countries **outside of the United States** (such as with respect to the approval of our product candidates), may materially and adversely impact our business, prospects, operating results, and financial condition. We or third parties upon whom we depend may be adversely affected by natural disasters and / or health epidemics, and our business, financial condition and results of operations could be adversely affected. Natural disasters could severely disrupt our operations and have a material adverse effect on our business operations. If a natural disaster, health epidemic, or other event beyond our control occurred that prevented us from using all or a significant portion of our office, manufacturing and / or lab spaces, that damaged critical infrastructure, such as the manufacturing facilities of our third- party contract manufacturers, or that otherwise disrupted operations, it may be difficult for us to continue our business for a substantial period of time. Any outbreak of contagious diseases, or other adverse public health developments, could have a material and adverse effect on our business operations. For example, during the COVID- 19 global pandemic, clinical site initiation and patient enrollment in our clinical trials were delayed due to prioritization of hospital resources in favor of COVID- 19 patients and difficulties in recruiting clinical site investigators and clinical site staff. ~~The~~ **Emerging or future variants of** COVID- 19 **, and other local or** global ~~pandemic~~ **health issues** , ~~including emerging or future variants of COVID- 19,~~ and ~~its~~ **could** impact ~~on our business is highly uncertain and subject to change. We do not yet know the full extent of potential delays or long- term impacts on~~ our business, our preclinical studies and clinical trials, healthcare systems or the global economy. In addition, certain of our research and development efforts are conducted globally. A health epidemic or other outbreak could materially and adversely affect our business, financial condition and results of operations. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. There is a substantial risk of product liability claims in our business. If we are unable to obtain or maintain sufficient insurance, a product liability claim against us could adversely affect our business. Our business exposes us to significant potential product liability risks that are inherent in the development, testing, manufacturing and marketing of human therapeutic products. Product liability claims could delay or prevent completion of our clinical development programs. In addition, if any of our collaboration partners face product liability claims, our programs could also be affected and our business could be harmed. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs, and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used, or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management' s time and our resources, substantial monetary awards to trial participants or patients and a decline in our share price. Any insurance we obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain or maintain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could adversely affect our business. If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected. Our research, development and manufacturing processes involve the use of hazardous materials. We maintain quantities of various flammable and toxic chemicals in our facilities that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Our procedures for storing, handling and disposing of these materials are reviewed against the relevant guidelines and laws of the jurisdictions in which our facilities are located on a regular basis. Although we believe that our safety procedures for handling and disposing of these materials sufficiently mitigate the risk of accidental contamination or injury from these materials, the risk cannot be completely eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood- borne pathogens and the handling of biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials. Additional federal, state and local laws and regulations affecting our operations may become applicable in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate any of, these laws or regulations.

Risks Related to Our Dependence on Third Parties We depend on collaborations with third parties for the development and commercialization of certain of our product candidates. We depend on third- party collaborators for the co- development and co-commercialization of certain of our product candidates and we face significant competition to the extent we elect to collaborate with others. Our potential future collaborators include large and mid- size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, there have been a significant number of business combinations among these companies that have resulted in a reduced number of potential future collaborators. In January 2023, we commenced a collaboration with GSK to research, develop, and commercialize oligonucleotide therapeutics, including WVE- 006, our ~~preclinical,~~ first- in- class A- to- I (G) RNA editing candidate for AATD. In April 2018, we commenced a collaboration with Takeda to discover, develop and commercialize oligonucleotides for disorders of the CNS. The collaboration provides Takeda with the option to globally co- develop and commercialize **a** ~~programs~~ **program** targeting HD ~~, ALS, FTD, and SCA3~~, which we will have the right to co- commercialize in the United States. Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. We may also be restricted under existing license or collaboration agreements from entering into agreements on certain terms with other potential collaborators. If we are unable to enter into collaborations with respect to a product candidate, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, 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 may 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 may not be able to further develop our product candidates or bring them to market and generate product revenue. Depending on the type of collaborations we enter into, we may have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates may pose the following risks to us: • collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations; • collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator' s strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; • collaborators may require us to enter into collaboration agreements that contain exclusivity provisions and / or termination penalties; • a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products; • collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation; • disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. Further, if a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. We may not be able to execute our business strategy optimally if we are unable to maintain our existing collaborations or enter into new collaborations with partners that can provide sales, marketing and distribution capabilities and funds for the development and commercialization of our product candidates. We do not currently have any sales and marketing or distribution capabilities. Accordingly, we entered into collaborations with GSK and Takeda, which we believe can assist us in building these capabilities. We may also enter into additional alliances in the future. We have selectively chosen to enter into our strategic collaborations because we believe this is the optimal way for us to leverage our resources and create significant value for ourselves and our shareholders, as we advance oligonucleotide candidates for genetically defined diseases. Depending on the collaborations that we enter into, we may expect our collaborators to provide assistance with development, regulatory affairs, marketing, sales and distribution, among other areas. Our future revenues may depend heavily on the success of the efforts of these third parties. For example, under our collaboration with Takeda, if Takeda exercises its option with respect to ~~any of~~ our ~~programs~~ **program** in HD ~~, ALS, FTD or SCA3~~, we will rely on Takeda for commercialization of such optioned programs outside of the United States. Under our collaboration with GSK, GSK is responsible for later clinical development and commercialization of our program in AATD. We may not be successful in our collaborations due to various factors, including our ability to successfully demonstrate proof of mechanism in humans, our ability to demonstrate the safety and efficacy of our specific product candidates, our ability to manufacture or have third parties manufacture our product candidates, the strength of our intellectual property and / or concerns about potential challenges to or limitations of our intellectual property. To the extent we have entered into, or enter into new, collaborations, we may not be able to maintain them if, for example, development or approval of a product candidate is delayed, challenges are raised as to the validity or scope of our intellectual property or sales of an approved drug are lower than we or our collaboration partner expected. For certain product candidates that we may develop, we have formed collaborations to fund all or part of the costs of

drug development and commercialization, such as our collaborations with GSK and Takeda. We may not, however, be able to enter into additional collaborations for certain other programs, and the terms of any collaboration agreement we do secure may not be favorable to us. If we are not successful in our efforts to enter into future collaboration arrangements with respect to one or more of our product candidates, we may not have sufficient funds to develop that or any other product candidate internally, or to bring any product candidates to market. If we do not have sufficient funds to develop and bring our product candidates to market, we will not be able to generate sales revenues from these product candidates, and this will substantially harm our business. We rely, and expect to continue to rely, on third parties to conduct some aspects of our compound formulation, research, preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such formulation, research or testing. We do not independently conduct all aspects of our drug discovery activities, compound formulation research, preclinical studies, or clinical trials of product candidates. We currently rely, and expect to continue to rely, on third parties to conduct some aspects of our research and development, preclinical and clinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our **preclinical** studies that ~~support~~ **supports** our ~~clinical trial applications~~ **INDs / CTAs is conducted in accordance with GLP requirements** and **, likewise, that** our clinical trials are conducted in accordance with GCP **requirements** , the study plan and ~~protocols~~ **protocol** for ~~the~~ **each** trial. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us or our strategic alliance partners to select viable product candidates for ~~clinical trial application~~ **IND / CTA** submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates. We rely on third parties to design, conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business. We rely on third party clinical investigators, CROs, clinical data management organizations and consultants to design, conduct, supervise and monitor preclinical studies and clinical trials of our product candidates. Because we rely on third parties and do not have the ability to conduct preclinical studies or clinical trials independently, we have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would if we conducted them on our own, including our inability to control whether sufficient resources are applied to our programs. If any of our CROs are acquired or consolidated, these concerns are likely to be exacerbated and our preclinical studies or clinical trials may be further impacted due to potential integration, streamlining, staffing and logistical changes. These investigators, CROs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. Further, these third parties may not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful. If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our preclinical and clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the **study or** trial. The FDA and other health authorities require clinical trials to be conducted in accordance with GCP, including conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. If we or our CROs fail to comply with these requirements, the data generated in our clinical trials may be deemed unreliable or uninterpretable **,** and the FDA and other health authorities may require us to perform additional clinical trials. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could adversely affect our business, financial condition, results of operations and prospects. We rely on third parties in the supply and manufacture of our product candidates for our research, preclinical and clinical activities, and may do the same for commercial supplies of our product candidates. While we have built our own internal manufacturing capabilities, we have not yet manufactured our product candidates on a commercial scale ~~,~~ and may not be able to do so for any of our product candidates. In addition, we currently rely on third parties in the supply and manufacture of materials for our research, preclinical and clinical activities and may continue to do so for the foreseeable future. We may do the same for the commercial supply of our drug product. We use third parties to perform additional steps in the manufacturing process, such as the filling, finishing and labeling of vials and storage of our product candidates and we expect to do so for the foreseeable future. There can be no assurance that our supply of research, preclinical and clinical development drug candidates and other materials will not be limited, interrupted or restricted or will be of satisfactory quality or continue to be available at acceptable prices. Replacement of any of the third parties we may engage could require significant effort and expertise because there may be a limited number of qualified replacements. In addition, raw materials, reagents, and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available, may not be suitable or acceptable for use due to material or component defects, or may introduce variability into the supply of our product candidates. Furthermore, with the increase of companies developing **oligonucleotides** ~~nucleic acid therapeutics~~ , there may be increased competition for the supply of the raw materials that are necessary to make our oligonucleotides, which could severely impact the manufacturing of our product candidates. We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and they must be acceptable to the FDA or approved by foreign regulatory authorities **.** Suppliers and manufacturers, including us, must meet applicable manufacturing requirements, including compliance

with cGMP regulations, and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards. In the event that any of our suppliers or manufacturers fail to comply with such requirements or to perform their obligations to us in relation to quality, timing or otherwise, some of which may be out of their or our control, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to increase the manufacturing of the materials ourselves, for which we currently have limited capabilities and resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. Any interruption of the development or operation of the manufacturing of our product candidates, such as order delays for equipment or materials, equipment malfunction, quality control and quality assurance issues, regulatory delays and possible negative effects of such delays on supply chains and expected timelines for product availability, production yield issues, shortages of qualified personnel, discontinuation of a facility or business or failure or damage to a facility resulting from natural disasters, could result in the cancellation of shipments, loss of product in the manufacturing process or a shortfall in available product candidates or materials. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. We may rely on third- party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. In complying with the manufacturing regulations of the FDA and other comparable foreign regulatory authorities, we and our third- party manufacturers must spend significant time, money, and effort in the areas of design and development, testing, production, record- keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. Although our agreements with third- party manufacturers require them to perform according to certain cGMP requirements such as those relating to quality control, quality assurance and qualified personnel, we cannot control the conduct of our third- party manufacturers to implement and maintain these standards. If any of our third- party manufacturers cannot successfully manufacture material that conforms to our specifications and the regulatory requirements of the FDA, or other comparable foreign authorities, we would be prevented from obtaining regulatory approval for our drug candidates unless and until we engage a substitute supplier that can comply with such requirements, which we may not be able to do. In addition, we and our third- party manufacturers responsible for the manufacture of commercial supplies of our products for which we retain regulatory approval, if any, are subject to inspection and approval by regulatory authorities before we may commence the manufacture and sale of any of such products, and thereafter are subject to ongoing inspection from time to time. Our third-party manufacturers may not be able to comply with applicable cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Any such failure by us or any of our suppliers would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved. We may also be required to enter into long- term manufacturing agreements that contain exclusivity provisions and / or substantial termination penalties which could have a material adverse effect on our business prior to or after commercialization of any of our product candidates. If we are unable to obtain or maintain third- party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Failure to execute on our manufacturing requirements, either by us or by one of our third- party vendors, could adversely affect our business in a number of ways, including: • an inability to initiate or continue clinical trials of product candidates under development; • delays in submitting regulatory applications, or receiving regulatory approvals, for product candidates; • loss of the cooperation of a collaborator; • additional inspections by regulatory authorities; • requirements to cease distribution or to recall batches of our product candidates; and • in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products. If any of our product candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own, or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to commercialize successfully any such future products. We currently have no sales, marketing or distribution capabilities. In addition, while our collaboration with Takeda and GSK will provide us with know- how and experience related to commercialization, we have limited experience of our own. If any of our product candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time- consuming, or rely on or enter into additional collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our products or decide to co- promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third- party marketing or distribution arrangements, any revenue we may receive will depend

upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects would be adversely affected. Risks Related to Managing Our Operations If we are unable to attract and retain qualified key management and scientists, staff, consultants and advisors, our ability to implement our business plan may be adversely affected. We are highly dependent upon our senior management and our scientific, clinical and medical staff and advisors. The loss of the service of any of the members of our senior management or other key employees could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. In addition, we expect that we will continue to have an increased need to recruit and hire qualified personnel as we advance our programs and expand operations. Failure to successfully recruit and retain personnel could impact our anticipated development plans and timelines. For example, in 2019, as a result of the stock price decline and our workforce reduction following the announcement of our decision to discontinue **one** ~~our development~~ of **our programs** ~~suvodirsen in DMD~~, we have faced challenges in retaining and attracting employees to support our research and development efforts, and our failure to do so could have an adverse effect on our ability to execute on our business plan. We are dependent on the continued service of our technical personnel because of the highly technical and novel nature of our product candidates, platform and technologies and the specialized nature of the regulatory approval process. Replacing such personnel may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully execute our business strategy, and we cannot assure you that we will be able to identify or employ qualified personnel for any such position on acceptable terms, if at all. Many of the biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain highly qualified scientific, technical and management personnel, as well as personnel with expertise in preclinical and clinical testing, manufacturing, governmental regulation and commercialization. In order to do so, we may need to pay higher compensation or fees to our employees or consultants than we currently expect, and such higher compensation payments may have a negative effect on our operating results. We face increased competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations. If we are unable to attract and retain qualified personnel, the rate and success at which we may be able to discover and develop our product candidates and implement our business plan will be limited. As we continue our preclinical studies and clinical trials and advance to further clinical development, we may experience difficulties in managing our growth and expanding our operations. Although we have assembled a team of employees with experience developing medicines and obtaining regulatory approval to market those medicines, we have limited experience as a company in drug development. We ~~have~~ **are** a **clinical** ~~robust and diverse pipeline of PN- modified, stereopure~~ **stage biotechnology company focused on unlocking the broad potential of RNA medicines (also known as** oligonucleotides **)** , ~~including programs using our~~ **or those targeting ribonucleic acid (RNA), to transform human health. Our RNA medicines platform, PRISM, combines multiple modalities, chemistry innovation and deep insights into human genetics to deliver scientific breakthroughs that treat both rare and prevalent disorders. Our toolkit of RNA- targeting modalities includes RNA** editing, splicing, ~~and~~ **antisense** silencing ~~modalities~~ **and RNA interference, providing us with unique capabilities for designing and sustainably delivering candidates that optimally address disease biology** . Our lead ~~clinical~~ programs are ~~focused~~ in ~~,~~ **rare** and **prevalent** ~~aim to address, muscle~~ diseases ~~(~~**, including AATD, obesity,** DMD ~~– splicing)~~ , ~~hepatic diseases (AATD – editing),~~ and ~~CNS diseases (~~HD ~~, ALS and FTD – silencing)~~ . As we advance product candidates through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In addition, we must manage our relationships with collaborators or partners, suppliers and other organizations, including our collaborations with GSK and Takeda. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. In addition, our future growth may require significant capital expenditures and may divert financial resources from other projects, such as the development of our product candidates. If we are unable to effectively manage our future growth, our expenses may increase and our ability to generate revenue could be reduced. Our employees, consultants and collaborators may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk of fraud and other misconduct by our employees, consultants and collaborators. Such misconduct could include intentional failures to comply with FDA and other foreign agency regulations, provide accurate information to the FDA, comply with manufacturing standards required by the FDA or us, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or

regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. Security breaches, ~~cyber security~~ **cybersecurity** threats, loss of data and other disruptions could compromise sensitive information related to our business, prevent us from accessing critical information or expose us to liability, which could adversely affect our business and our reputation. In the ordinary course of our business, we, our CROs and other third parties, including our managed service providers (" MSPs "), on which we rely collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, vendor information, and proprietary business information. We, along with our MSPs, manage and maintain our applications and data utilizing cloud- based and on- site systems. These applications and data encompass a wide variety of business- critical information, including research and development information and business and financial information. The secure processing, storage, maintenance and transmission of this critical information by us, or our CROs and other third **- party** ~~parties~~ **partners** ~~with whom Wave does business~~, is vital to our operations and business strategy. We also have systems in place at our facilities to mitigate disruptions to our communications systems, including the prevention of a loss to our electrical systems. Although we are proactive in our approach and take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure, or that of our CROs or other third party partners, may be vulnerable to attacks by hackers, viruses, breaches, interruptions due to employee error, malfeasance or other disruptions, lapses in compliance with privacy and security mandates, or damage from natural disasters, terrorism, war and telecommunication and electrical failures. For example, ~~the COVID- 19 pandemic has~~ **as** ~~led to~~ **previously disclosed in May 2023** ~~an~~ **and August 2023** ~~increase in those working remotely~~, ~~including~~ **we became aware that our mHTT assay vendor experienced a cybersecurity incident in April 2023. None of our data** ~~our~~ **or** ~~employees~~ **patient samples were impacted by the incident** and ~~third parties~~ **we remain in close contact** with **the vendor** ~~whom we do business, which increases our cyber security risk. This increased risk has~~ **as** ~~created data accessibility concerns~~ **they address this issue. The financial impact of this incident was not material,** and **there were no changes** ~~has made us more susceptible~~ to ~~communication disruptions~~ **the previously released financial results or financial statements**. In addition, cyberattacks, malicious internet- based activity and fraud are prevalent and continue to increase in frequency. Any such event, including a cyberattack, could compromise our networks, or that of our CROs or other third parties, and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen. Furthermore, any such event could **subject us to liability, negatively impact our business operations, or** result in information theft, data corruption, operational disruption, damage to our reputation, or financial loss ~~, and could subject us to liability or negatively impact our business operations~~. As part of our robust data protection practices, we regularly conduct business continuity and disaster recovery testing of our key information systems and data. We have measures in place that are designed to detect and respond to such security incidents and breaches of privacy and security mandates. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information (including **but not limited to** GDPR, HIPAA and HITECH ~~, among others~~), government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also **adversely affect our business, damage our reputation, and** disrupt our operations, including our ability to conduct research and development activities, process and prepare company financial information, **and** manage various general and administrative aspects of our business ~~and damage our reputation, any of which could adversely affect our business~~. For example, the loss of **intellectual property or** clinical trial data from completed or ongoing **or planned** clinical trials, in addition to privacy concerns, could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, while we take measures to help ensure early detection, there can be no assurance that we, or our CROs and other third party partners, will promptly detect any such disruption or security breach, if at all. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed. Numerous federal, state and international laws address privacy, data protection and the collection, storing, sharing, use, disclosure and protection of personally identifiable information and other user data. ~~Numerous~~ **In the United States, several** states **have** already ~~have, and~~ **implemented state laws addressing privacy or** are ~~looking~~ **set** to **enact** ~~expand,~~ data protection legislation. **As** ~~For example, in 2018, California enacted~~ the **patchwork of U** ~~California Consumer Privacy Act (" CCPA "), which became effective on January 1, 2020 giving California residents expanded privacy rights and protections and imposing fines and penalties~~. **S.** ~~2023 will also see new~~ privacy laws **expands** ~~in Virginia (effective January 1~~, ~~2023), Connecticut (effective July 1, 2023), Colorado (effective July 1, 2023), and Utah (effective December 31, 2023). Each year, many~~ state ~~legislatures continue to consider similar privacy laws, further expanding the patchwork of US privacy laws. State~~ enforcement of data privacy and cybersecurity breaches has increased, along with the cost. ~~California issued its first fine under the CCPA in the amount of $ 1. 2 million, and the New York Attorney General has enforced its NY SHIELD Act by fining companies over $ 3, 000, 000.~~ In addition **to state enforcement of privacy laws**, the Federal Trade Commission has ~~zeroed in on~~ **increased enforcement of cybersecurity and** data privacy ~~and security as a central role~~, and **related fines in** 2023 ~~may see increased enforcement and regulation~~. Outside the United States, personally identifiable information and other user data is increasingly subject to legislation and regulations in numerous jurisdictions around the world, the intent of which is to protect the privacy of information that is collected, processed and transmitted in or from the governing jurisdiction. Foreign data protection, privacy, information security, user protection and other laws and regulations are often more restrictive than those in the United States. For example, ~~in April 2016, European legislative bodies adopted~~ the General Data Protection Regulation (" GDPR ") **adopted by the European legislative bodies** ~~, which became effective May 25, 2018, and which~~ applies to any company, regardless of location, that collects or processes personal data of EU residents in connection with offering goods or services in the ~~EU~~ **European Union** or monitoring the behavior of EU residents. The GDPR enhances data protection obligations for processors and controllers of personal data,

including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, data minimization obligations, record- keeping requirements, mandatory data breach notification requirements, and correlated obligations on services providers. The GDPR also strictly regulates cross- border transfer of personal data, including requirements for data transfer impact assessments. Non- compliance with the GDPR may result in monetary penalties of up to € 20 million or 4 % of annual worldwide revenue, whichever is higher. **Additionally** ~~In addition~~ , post- Brexit the ~~UK~~ **United Kingdom** has also adopted its own version of the GDPR ~~, which requires additional compliance measures~~ . While we have taken steps to comply with **all** applicable privacy laws and regulations, including the GDPR, by taking measures including **but not limited to** enhancing our security procedures, updating our website, revising our clinical trial informed consents, adopting the standard contractual clauses for cross- border transfers of personal data **, increasing our cyber insurance** , and entering into data processing agreements with relevant CROs and third party partners, we cannot **completely** assure you that our efforts to remain in compliance will be fully successful. The GDPR and other changes in laws or regulations associated with the enhanced protection of personal data may increase our costs of compliance and result in greater legal risks. Foreign currency exchange rates may adversely affect our results. Due to our operations outside of the United States, we are exposed to market risk related to changes in foreign currency exchange rates. Historically, we have not hedged our foreign currency exposure. Changes in the relative values of currencies occur regularly and, in some instances, could materially adversely affect our business, our financial condition, the results of our operations or our cash flows. For the years ended December 31, **2023 and** 2022 ~~and 2021~~ , changes in foreign currency exchange rates did not have a material impact on our historical financial position, our business, our financial condition, the results of our operations or our cash flows. A hypothetical 10 % change in foreign currency rates would not have a material impact on our historical financial position or results of operations. However, there can be no assurance that changes in foreign currency exchange rates will not have a material adverse impact on us in the future. The U. S. tax legislation and future changes to applicable U. S. or foreign tax laws and regulations may have a material adverse effect on our business, financial condition and results of operations. We are subject to income and other taxes in the United States and foreign jurisdictions. Changes in laws and policy relating to taxes or trade, including increases in tax rates or modifications, technical corrections or clarifications to tax laws, such as the Tax Cuts and Jobs Act of 2017, which eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over a period of years, may have an adverse effect on our business, financial condition and results of operations. This Annual Report on Form 10- K does not discuss any such tax legislation or changes to tax laws and legislation, or the manner in which it might affect us or purchasers of our securities. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our securities. We are also subject to different tax regulations in each of the jurisdictions where we conduct our business or where our management is located. We expect the scope and extent of regulation in the jurisdictions in which we conduct our business, or where our management is located, as well as regulatory oversight and supervision, to generally continue to increase. Generally, future changes in applicable U. S. or foreign tax laws and regulations, or their interpretation and application could have an adverse effect on our business, financial condition and results of operations. Inadequate funding for the FDA, the SEC and other government agencies, or a work slowdown or stoppage at those agencies as part of a broader federal government shutdown, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also extend the time necessary for new drugs to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. ~~Additionally, the FDA and regulatory authorities outside the United States have imposed and may continue to impose various restrictions or other policy measures in response to the COVID- 19 pandemic.~~ If a prolonged government shutdown or slowdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Risks Related to Our Intellectual Property If we are not able to obtain and enforce market exclusivity for our technologies or product candidates, development and commercialization of our product candidates may be adversely affected. In our industry, the majority of an innovative product' s commercial value is usually realized during the period in which it has market exclusivity. Market exclusivity is comprised of both patent and other intellectual property protection, as well as regulatory exclusivity. In the United States and some other countries, when market exclusivity expires and generic versions of a product are approved and marketed, there usually are very substantial and rapid declines in the product' s sales. Accordingly, our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including trademarks, trade secrets and in- licenses of intellectual property rights of others, for our product candidates and platform technologies, methods used to manufacture our product candidates, methods of patient stratification and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. Certain research and development activities involved in pharmaceutical development are exempt from patent infringement in the United States and other jurisdictions, for example, in

the United States by the provisions of 35 U. S. C. § 271 (e) (1) (the " Safe Harbor "). However, in the United States and certain other jurisdictions, the Safe Harbor exemption terminates when the sponsor submits an application for marketing approval (e. g., a New Drug Application (" NDA ") in the United States). Therefore, the risk that a third party might allege patent infringement may increase as our products approach commercialization. We may not be able to apply for patents or obtain patent protection on certain aspects of our product candidates or our platform in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable, or that any issued or granted patents will include claims that are sufficiently broad to cover our product candidates, our platform technologies, or any methods relating to them, or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain and involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market. Legal issues related to the patentability of biopharmaceuticals, and methods of their manufacture and use, are complex and uncertain in some countries. In some countries, applicants are not able to protect methods of treating human beings or medical treatment processes. Intellectual property protection varies throughout the world and is subject to change over time. Certain jurisdictions have enacted various rules and laws precluding issuance of patents encompassing any methods a doctor may practice on a human being or any other animal to treat a disease or condition. Further, many countries have enacted laws and regulatory regimes that do not allow patent protection for methods of use of known compounds. Particularly given that some of our product candidates may represent stereopure versions of previously described oligonucleotides, it may be difficult or impossible to obtain patent protection for them in relevant jurisdictions. Thus, in some countries and jurisdictions, it may not be possible to patent some of our product candidates at all. In some countries and jurisdictions, only composition claims may be obtained, and only when those compositions are or contain compounds that are new and / or novel. Also, patents issued with composition claims (i. e., covering product candidates) cannot always be enforced to protect methods of using those compositions to treat or diagnose diseases or medical conditions. In such countries or jurisdictions, enforcement of patents to protect our product candidates, or their uses, may be difficult or impossible. Lack of patent protection in such cases may have a materially adverse effect on our business and financial condition. Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates, their manufacture or their use might expire before or shortly after those candidates receive regulatory approval and are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms where these are available upon regulatory approval in those countries where we are prosecuting patents. This includes in the United States under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent term extension of up to five years beyond the expiration of the patent. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be possible. The U. S. Patent and Trademark Office (" USPTO ") and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent prosecution process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, or loss of right to enforce patent claims, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not uniform, can vary substantially from country to country, and are not always applied predictably, requiring country- specific patent expertise in each jurisdiction in which patent protection is sought. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technologies. While we will endeavor to try to protect our product candidates and platform technology with intellectual property rights such as patents, as appropriate, the process of filing and prosecuting patent applications, and obtaining, maintaining and defending patents is time-consuming, expensive, uncertain, and sometimes unpredictable. In addition, periodic changes to the patent laws and rules of patent offices around the world, including the USPTO can have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the America Invents Act, enacted in 2011, involved significant changes in patent legislation. Furthermore, the U. S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The 2013 decision by the U. S. Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc. precludes a claim to a nucleic acid having a stated nucleotide sequence which is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing oligonucleotides which contain modifications that we believe are not found in nature. However, we cannot make assurances that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. 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 the U. S. Congress, the federal courts and the USPTO, and by analogous bodies around the world, 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. For example, in 2012, European countries and the European Parliament agreed to a legislative package that would create a unitary patent protection system in the EU; aspects of this system **were** ~~are scheduled to be~~ implemented beginning in 2023 for at least some European countries. The impact of the proposed unitary patent protection system on patents in Europe is currently unclear. Once granted, patents may remain open to opposition, interference, re- examination, post- grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims attacked or may lose the allowed or granted claims altogether. In addition, there can be no assurance that: • Others will not or may not be able to make, use or sell compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or license. • We or our licensors, collaborators or any future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license. • We or our licensors, collaborators or any future collaborators are the first to file patent applications covering certain aspects of our inventions. • Others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights. • A third party may not challenge, invalidate, circumvent or weaken our patents, or that, if any of these events should occur, that a court would hold that our patents are valid, enforceable and infringed. • Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged, invalidated, circumvented or weakened by third parties. • We may develop additional proprietary technologies that are patentable. • The patents of others will not have an adverse effect on our business. • Our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets. We license patent rights from third- party owners or licensees. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected. We license patent rights from third parties that we may use from time to time to protect certain aspects of our technology and programs. We may license additional third- party intellectual property in the future. To the extent that we use, and ultimately rely on, in- licensed technologies in our platform and our programs, our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for those in- licensed technologies. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing products. Without protection for, or exclusive right to, the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we may sublicense our rights under our third- party licenses to current or future collaborators or any future strategic partners. Any impairment of these sublicensed rights could result in reduced revenue under any future collaboration agreements we may enter into or result in termination of an agreement by one or more of our current or future collaborators or any future strategic partners. Other companies or organizations may challenge our or our licensors' patent rights or may assert patent rights that prevent us from developing and commercializing our products. Nucleic acid therapeutics is a relatively new scientific field, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of patents in this field. The issued patents and pending patent applications in the United States and in key markets around the world that we own or license claim certain methods, compositions and processes relating to the discovery, development, manufacture and / or commercialization of oligonucleotides and / or our platform. As the field of oligonucleotides matures, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation in the courts and other proceedings, such as interference, reexamination and opposition proceedings, in various patent offices relating to patent rights in the oligonucleotides field. In many cases, the possibility of appeal or opposition exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is uncertain and may adversely affect our business, particularly if we are not successful in defending the patentability and scope of our pending and issued patent claims or if third parties are successful in obtaining claims that cover any of our product candidates or our platform. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, invalidated or circumvented, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to challenge, invalidate, circumvent or weaken our intellectual property rights could be costly to us, could require significant time and attention of our management and could adversely affect our business and our ability to successfully compete in the field of oligonucleotides. We may not be able to protect our intellectual property rights throughout the world. Obtaining a valid and enforceable issued or granted patent covering our technology in the United States and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the United States. Competitor products may compete with our future products in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property

protection, particularly relating to biopharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. We generally file a provisional patent application first (a priority filing) at the USPTO. A Patent Cooperation Treaty (" PCT ") application is usually filed within 12 months after the priority filing. Regional and / or national patent applications may be pursued outside of the United States, either based on a PCT application or as a direct filing, in some cases claiming priority to a prior U. S. or PCT filing. Some of our cases have been filed in multiple jurisdictions, including major market jurisdictions. We also commonly enter the national stage in the United States through a PCT filing. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that depending on the country, different scopes of patent protection may be granted on the same product or technology. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties, allowing competitors to manufacture and sell their own versions of our product, thereby reducing our sales. In addition, many countries do not permit enforcement of patents, or limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such a patent. If we or any of our licensors, collaborators or present or future partners are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected. The requirements for patentability may differ in certain countries. For example, some jurisdictions may have heightened requirements for patentability compared to others, and may specifically require a detailed description of medical uses of a claimed drug. In some jurisdictions, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' or collaborators' patents, requiring us or our licensors or collaborators to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch generic versions of our products. Accordingly, our and our licensors' and collaborators' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. We or our licensors, collaborators or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly and time consuming, or delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk. We or our licensors, collaborators or any future strategic partners may be subject to third- party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors or collaborators for damages arising from intellectual property infringement by us. If we or our licensors, collaborators or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, collaborators or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non- exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or our collaborator, or any future collaborator, may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management' s attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations. If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, lack of written disclosure, obviousness, or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal allegations of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform

technology. Such a loss of patent protection could negatively impact our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights. Intellectual property rights of third parties could adversely affect our ability to commercialize our product candidates, and we might be required to litigate or obtain licenses from third parties in order to develop or market our product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms. Because the oligonucleotide intellectual property landscape is still evolving and our product candidates have not yet reached commercialization, it is difficult to conclusively assess our freedom to operate. There are numerous companies that have pending patent applications and issued patents directed to certain aspects of oligonucleotides. We are aware of third-party competitors in the oligonucleotide therapeutics space, whose patent filings and / or issued patents may include claims directed to targets and / or products related to some of our programs. It is possible that at the time that we commercialize our products these third- party patent portfolios may include issued patent claims that cover our products or critical features of their production or use. Our competitive position may suffer if patents issued to third parties or other third- party intellectual property rights cover, or may be alleged to cover, our products or elements thereof, or methods of manufacture or use relevant to our development plans. In such cases, we may not be in a position to develop or commercialize product candidates unless we successfully pursue litigation to nullify or invalidate the third party intellectual property right concerned or enter into a license agreement with the intellectual property right holder, if available on commercially reasonable terms. It is also possible that we have failed to identify relevant third- party patents or applications. For example, U. S. applications filed before November 29, 2000, and certain U. S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing date for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products. Third party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time- consuming litigation and may be prevented from or experience substantial delays in marketing our products. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product candidates that are held to be infringing. We might, if possible, also be forced to redesign product candidates so that we no longer infringe the third- party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. If we fail to comply with our obligations under any license, collaboration or other agreement, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates, or we could lose certain rights to grant sublicenses. There are many issued patents and / or pending patent applications that claim aspects of oligonucleotide compositions, chemistry and / or modifications that we may want or need to apply to our product candidates. There are also many issued patents and / or pending patent applications that claim targeted genes or portions of genes that may be relevant for the oligonucleotides we wish to develop. We are aware of third- party competitors in the oligonucleotide therapeutics space whose patent filings and / or issued patents may include claims directed to targets and / or product candidates related to some of our development programs. It is possible that these third- party patent portfolios may include issued patent claims that cover our product candidates or critical features of their production or use. Thus, it is possible that one or more organizations will hold patent rights to which we will need or want a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, or at all, we may not be able to market products or perform research and development or other activities covered by these patents. Our technology licenses and any future licenses we enter into are likely to impose various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and / or other obligations on us. If we breach any of these imposed obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. 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 protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patent protection for certain aspects of our product candidates, we also consider trade secrets, including confidential and unpatented know- how, improvements and technological innovation important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know- how, improvements and technological innovation, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a

party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel. Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. 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 trademarks or trade names may be infringed, challenged, invalidated, circumvented, weakened or declared generic 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. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. Risks Related to Our Being a Singapore Company We are a Singapore incorporated company and it may be difficult to enforce a judgment of U. S. courts for civil liabilities under U. S. federal securities laws against us, our directors or our officers in Singapore. We are incorporated under the laws of the Republic of Singapore, and certain of our directors are residents outside the United States. Moreover, a significant portion of our consolidated assets are located outside the United States. Although we are incorporated outside the United States, we have agreed to accept service of process in the United States through our agent designated for that purpose. Nevertheless, because a majority of the consolidated assets owned by us are located outside the United States, any judgment obtained in the United States against us may not be enforceable within the United States. There is no treaty between the United States and Singapore providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters and a final judgment for the payment of money rendered by any federal or state court in the United States based on civil liability, whether or not predicated solely upon the federal securities laws, would, therefore, not be automatically enforceable in Singapore. There is uncertainty as to whether judgments of courts in the United States based upon the civil liability provisions of the federal securities laws of the United States would be recognized or enforceable in Singapore. In addition, holders of book- entry interests in our shares will be required to be registered shareholders as reflected in our shareholder register in order to have standing to bring a shareholder action and, if successful, to enforce a foreign judgment against us, our directors or our executive officers in the Singapore courts. The administrative process of becoming a registered holder could result in delays prejudicial to any legal proceedings or enforcement action. Consequently, it may be difficult for investors to enforce against us, our directors or our officers in Singapore judgments obtained in the United States which are predicated upon the civil liability provisions of the federal securities laws of the United States. We are incorporated in Singapore and our shareholders may have more difficulty in protecting their interests than they would as shareholders of a corporation incorporated in the United States. Our corporate affairs are governed by our constitution and by the laws governing corporations incorporated in Singapore. The rights of our shareholders and the responsibilities of the members of our board of directors under Singapore law are different from those applicable to a corporation incorporated in the United States. Principal shareholders of Singapore companies do not owe fiduciary duties to minority shareholders, as compared, for example, to controlling shareholders in corporations incorporated in Delaware. Our public shareholders may have more difficulty in protecting their interests in connection with actions taken by our management, members of our board of directors or our principal shareholders than they would as shareholders of a corporation incorporated in the United States. In addition, only persons who are registered as shareholders in our shareholder register are recognized under Singapore law as shareholders of our company. Only registered shareholders have legal standing to institute shareholder actions against us or otherwise seek to enforce their rights as shareholders. Investors in our shares who are not specifically registered as shareholders in our shareholder register (for example, where such shareholders hold shares indirectly through the Depository Trust Company) are required to become registered as shareholders in our shareholder register in order to institute or enforce any legal proceedings or claims against us, our directors or our executive officers relating to shareholder rights. Holders of book- entry interests in our shares may become registered shareholders by exchanging their book- entry interests in our shares for certificated shares and being registered in our shareholder register. Such process could result in administrative delays which may be prejudicial to any legal proceeding or enforcement action. We are subject to the laws of Singapore, which differ in certain material respects from the laws of the United States. As a company incorporated under the laws of the Republic of Singapore, we are required to comply with the laws of Singapore, certain of which are capable of extra-territorial application, as well as our constitution. In particular, we are required to comply with certain provisions of the Securities and Futures Act 2001 of Singapore (the " SFA "), which prohibit certain forms of market conduct and require certain information disclosures, and impose criminal and civil penalties on corporations, directors and officers in respect of any breach of such provisions. We are required to comply with the Singapore Code on Take- Overs and Mergers (the " Singapore Takeover Code "), which specifies, among other things, certain circumstances in which a general offer is to be made upon a change in

effective control, and further specifies the manner and price at which voluntary and mandatory general offers are to be made. We are also subject to Section 34 of the Singapore Patents Act, which provides that a person residing in Singapore is required to obtain written authorization from the Singapore Registrar of Patents (the " Registrar ") before filing an application for a patent for an invention outside of Singapore, unless certain conditions have been satisfied. A violation of Section 34 is a criminal offense punishable by a fine not exceeding S $ 5, 000, or imprisonment for a term not exceeding two years, or both. There have been some instances where we have undertaken filings outside of Singapore, and there may be instances where we are required to make such filings in the future, without first obtaining written authorization from the Registrar. We have notified the Registrar of such filings and we have since implemented measures to address the requirements of Section 34 moving forward. To date, the Registrar has offered a compound of some of the offences considered against payment of a sum of S $ 50 to S $ 150 per considered case. Under Singapore law, the Registrar has discretion to offer a compound of such offences against payment of a sum of money of up to S $ 2, 000, or to prosecute the offence subject to the other penalties noted above. Per requests in the Registrar' s most recent decision, we have submitted approximately 140 patent applications in multiple patent families, most of which are related to previously reported applications, to the Intellectual Property Office of Singapore (" IPOS "). The IPOS may consider the filing of some or all of these applications to have breached Section 34 requirements per IPOS' current interpretation of Section 34, and we are waiting for IPOS' decision on these applications. We cannot assure you that the Registrar will offer to compound any such violations of Section 34, or that any offer to compound will be for an amount similar to previous compound ~~offer~~ **offers** . The laws of Singapore and of the United States differ in certain significant respects. The rights of our shareholders and the obligations of our directors and officers under Singapore law (including under the Companies Act 1967 of Singapore (the " Singapore Companies Act ") are different from those applicable to a company incorporated in the State of Delaware in material respects, and our shareholders may have more difficulty and less clarity in protecting their interests in connection with actions taken by our management, members of our board of directors or our affiliated shareholders than would otherwise apply to a company incorporated in the State of Delaware. The application of Singapore law, in particular, the Singapore Companies Act may, in certain circumstances, impose more restrictions on us and our shareholders, directors and officers than would otherwise be applicable to a company incorporated in the State of Delaware. For example, the Singapore Companies Act requires directors to act with a reasonable degree of diligence and, in certain circumstances, imposes criminal liability for specified contraventions of particular statutory requirements or prohibitions. In addition, pursuant to the provisions of the Singapore Companies Act, shareholders holding 10 % or more of the total number of paid- up shares carrying the right of voting in general meetings may require the convening of an extraordinary general meeting of shareholders by our directors. If our directors fail to comply with such request within 21 days of the receipt thereof, the original requisitioning shareholders, or any of them holding more than 50 % of the voting rights represented by the original requisitioning shareholders, may proceed to convene such meeting, and we will be liable for the reasonable expenses incurred by such requisitioning shareholders. We are also required by the Singapore Companies Act to deduct such corresponding amounts from fees or other remuneration payable by us to such non- complying directors. We are subject to the Singapore Takeover Code, which requires a person acquiring 30 % or more of our voting shares to conduct a takeover offer for all of our voting shares. This could have the effect of discouraging, delaying or preventing a merger or acquisition and limit the market price of our ordinary shares. We are subject to the Singapore Takeover Code. The Singapore Takeover Code contains provisions that may delay, deter or prevent a future takeover or change in control of our company and limit the market price of our ordinary shares for so long as we remain a public company with more than 50 shareholders and net tangible assets of S $ 5 million (Singapore dollars) or more. For example, under the Singapore Takeover Code, any person acquiring, whether by a series of transactions over a period of time or not, either on **its** ~~such person' s~~ own or together with parties acting in concert with **it** ~~such person~~ , 30 % or more of our voting shares, or if such person holds, either on **its** ~~such person' s~~ own or together with parties acting in concert with **it** ~~such person~~ , between 30 % and 50 % (both inclusive) of our voting shares, and if such person (or parties acting in concert with **it** ~~such person~~ ) acquires additional voting shares representing more than 1 % of our voting shares in any six- month period, must, except with the consent of Securities Industry Council in Singapore, extend a takeover offer for our remaining voting shares in accordance with the Singapore Takeover Code. Therefore, any investor seeking to acquire a significant stake in our company may be deterred from doing so if, as a result, such investor would be required to conduct a takeover offer for all of our voting shares. These same provisions could discourage potential investors from acquiring a stake or making a significant investment in our company and may substantially impede the ability of our shareholders to benefit from a change of effective control and, as a result, may adversely affect the market price of our ordinary shares and the ability to realize any benefits from a potential change of control. For a limited period of time, our directors have general authority to allot and issue new ordinary shares on terms and conditions and for such purposes as may be determined by our board of directors in its sole discretion. Under Singapore law, we may only allot and issue new shares with the prior approval of our shareholders in a general meeting. At our most recent annual general meeting of shareholders, our shareholders provided our directors with a general authority, subject to the provisions of the Singapore Companies Act and our constitution, to allot and issue any number of new ordinary shares and / or make or grant offers, agreements, options or other instruments (including the grant of awards or options pursuant to our equity- based incentive plans and agreements in effect from time to time) that might or would require ordinary shares to be allotted and issued (collectively, the " Instruments "); and unless revoked or varied by us in a general meeting, such authority will continue in force until the earlier of (i) the conclusion of our next annual general meeting of shareholders, or (ii) the expiration of the period within which our next annual general meeting of shareholders is required by law to be held. Subject to the general requirements of the Singapore Companies Act and our constitution, the general authority given to our directors by our shareholders to allot and issue ordinary shares and / or make or grant the Instruments may be exercised by our directors on such terms and conditions, for such purposes and for consideration as they may in their sole discretion deem fit, and with such rights or restrictions as they may think fit to impose and as are set forth in our constitution. Any additional issuances of new ordinary

shares and / or any grant of the Instruments by our directors may dilute our shareholders' interests in our ordinary shares and / or adversely impact the market price of our ordinary shares. We may be or become a passive foreign investment company, which could result in adverse U. S. federal income tax consequences to U. S. Holders. The rules governing passive foreign investment companies (" PFICs ") can have adverse effects for U. S. federal income tax purposes. The tests for determining PFIC status for a taxable year depend upon the relative values of certain categories of assets and the relative amounts of certain kinds of income. The determination of whether we are a PFIC, which must be made annually after the close of each taxable year, depends on the particular facts and circumstances (such as the valuation of our assets, including goodwill and other intangible assets) and may also be affected by the application of the PFIC rules, which are subject to differing interpretations. The fair market value of our assets is expected to relate, in part, to (a) the market price of our ordinary shares and (b) the composition of our income and assets, which will be affected by how, and how quickly, we spend any cash that is raised in any financing transaction. Moreover, our ability to earn specific types of income that we currently treat as non- passive for purposes of the PFIC rules is uncertain with respect to future years. Based on our gross income, the average value of our assets, including goodwill and the nature of our active business, we do not expect to be treated as a PFIC for U. S. federal income tax purposes for the taxable year ended December 31, ~~2022~~ **2023** . Because the value of our assets for purposes of determining PFIC status will depend in part on the market price of our ordinary shares, which may fluctuate significantly, there can be no assurance that we will not be considered a PFIC for our current taxable year ending December 31, ~~2023~~ **2024** or for any future taxable year. If we are a PFIC, a U. S. Holder (defined below) would be subject to adverse U. S. federal income tax consequences, such as ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U. S. federal income tax laws and regulations. A U. S. Holder may in certain circumstances mitigate adverse tax consequences of the PFIC rules by filing an election to treat the PFIC as a qualified electing fund (" QEF ") or, if shares of the PFIC are " marketable stock " for purposes of the PFIC rules, by making a mark- to- market election with respect to the shares of the PFIC. If a U. S. Holder makes a mark- to- market election with respect to its ordinary shares, the U. S. Holder is required to include annually in its U. S. federal taxable income an amount reflecting any year end increase in the value of its ordinary shares. For purposes of this discussion, a " U. S. Holder " is a beneficial owner of ordinary shares that is for U. S. federal income tax purposes: (i) an individual who is a citizen or resident of the United States; (ii) a corporation (or other entity taxable as a corporation for U. S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia; (iii) an estate the income of which is subject to U. S. federal income taxation regardless of its source; or (iv) a trust (a) if a court within the U. S. can exercise primary supervision over its administration, and one or more U. S. persons have the authority to control all of the substantial decisions of that trust, or (b) that was in existence on August 20, 1996, and validly elected under applicable Treasury Regulations to continue to be treated as a domestic trust. Investors should consult their own tax advisors regarding all aspects of the application of the PFIC rules to the ordinary shares. Singapore taxes may differ from the tax laws of other jurisdictions. Prospective investors should consult their tax advisors concerning the overall tax consequences of purchasing, owning and disposing of our shares. Singapore tax law may differ from the tax laws of other jurisdictions, including the United States. We may become subject to unanticipated tax liabilities. We are incorporated under the laws of Singapore. **Under Singapore tax law, from January 1, 2024, subject to certain exceptions, gains from the sale or disposal by an entity without adequate economic substance and belonging to a relevant group of entities, of any movable or immovable property situated outside Singapore and that are received in Singapore from outside Singapore, are treated as income chargeable to tax.** We are **also** ~~, however,~~ subject to income, withholding or other taxes in certain jurisdictions by reason of our activities and operations, and it is also possible that tax authorities in any such jurisdictions could assert that we are subject to greater taxation than we currently anticipate. Any such **Singaporean and** non- Singaporean tax liability could materially adversely affect our results of operations. Tax authorities could challenge the allocation of income and deductions among our subsidiaries, which could increase our overall tax liability. We are organized in Singapore, and we currently have subsidiaries in the United States, Japan, the United Kingdom, and Ireland. As we grow our business, we conduct, and expect to continue to conduct, increased operations through our subsidiaries in various jurisdictions. If two or more affiliated companies are located in different jurisdictions, the tax laws or regulations of each country generally will require transactions between those affiliated companies to be conducted on terms consistent with those between unrelated companies dealing at arms' length, and appropriate documentation generally must be maintained to support the transfer prices. We maintain our transfer pricing policies to be compliant with applicable transfer pricing laws, but our transfer pricing procedures are not binding on applicable tax authorities. If tax authorities were to successfully challenge our transfer pricing, there could be an increase in our overall tax liability, which could adversely affect our financial condition, results of operations and cash flows. In addition, the tax laws in the jurisdictions in which we operate are subject to differing interpretations. Tax authorities may challenge our tax positions, and if successful, such challenges could increase our overall tax liability. In addition, the tax laws in the jurisdictions in which we operate are subject to change. We cannot predict the timing or content of such potential changes, and such changes could increase our overall tax liability, which could adversely affect our financial condition, results of operations and cash flows. Our financial results reflect the effect of certain tax credits and the operation of certain tax regimes within the United Kingdom. Legislation in the United Kingdom will limit the amount we may be able to claim as a payable tax credit in the future which could impact our financial condition, results of operations and cash flows. As a company that carries out extensive research and development activities, we benefit from the U. K. research and development tax credit regime for small and medium **-** sized companies, whereby our subsidiary in the United Kingdom is able to surrender the trading losses that arise from its research and development activities for a payable tax credit of up to 33. 4 % of eligible research and development expenditure on staff and consumables incurred on or before March 31, 2023 and generally up to 18. 6 % of such expenditure incurred on or after April 1, 2023. Expenditure of staff supplied by unconnected third parties incurred on or before March 31, 2023 are eligible for a cash rebate of up to 21. 7 % and generally up to 12. 1 % for such

expenditure incurred on or after April 1, 2023. Due to a change in the U. K. legislation affecting the U. K. research and development tax credit regime for small - and medium - sized companies, our ability to receive a payable tax credit for the surrender of our trading losses from research and development activities incurred from January 1, 2022 will be limited to the amount equal to three times our " pay as you earn " and U. K. national insurance tax liabilities, absent our qualification under an exception from such limitation. Further, we may not be able to continue to claim a U. K. tax credit for research and development tax credits under the small and medium- sized companies regime in the future if ~~we increase~~ **our revenue** ~~our~~ **or** ~~personnel~~ **turnover exceeds € 100 million for a second consecutive year. In such** ~~and~~ **an event,** ~~expand our business because~~ we ~~may~~ **will** no longer qualify as a small or medium- sized enterprise **. Recently proposed U. K. legislation would merge the small and medium- sized companies regime and the research and development expenditure credit (RDEC) regime generally for large companies. This legislation would generally apply a 20 % rate to qualifying R & D expenditures. The draft legislation also includes changes to other rules and types of qualifying expenditure, such as the treatment of subcontracted and overseas costs. We are currently evaluating the impact of the draft legislation on our future tax credit claims** . Risks Related to Our Ordinary Shares The public market for our ordinary shares may not be liquid enough for our shareholders to sell their ordinary shares quickly or at market price, or at all. Our ordinary shares are currently listed for trading on the Nasdaq Global Market. There is no assurance that the trading market for our shares will be or remain active. Our shareholders may not be able to sell their ordinary shares quickly or at the market price, or at all. Our executive officers, our directors and their respective affiliates, and our other significant shareholders beneficially own a significant portion of our outstanding ordinary shares, and therefore, liquidity in our ordinary shares is limited. Due to the limited liquidity in our ordinary shares, relatively small orders can have a disproportionate impact on the trading price of our shares. Further, the limited liquidity in our ordinary shares may also impair our ability to raise capital by conducting offerings of our ordinary shares and may impair our ability to enter into strategic partnerships or acquire companies or products by using our ordinary shares as consideration. The market price of our ordinary shares is likely to be highly volatile, and our shareholders may lose some or all of their investment. The market price of our ordinary shares is likely to continue to be highly volatile, including in response to factors that are beyond our control. The stock market in general experiences extreme price and volume fluctuations. In particular, the market prices of securities of pharmaceutical and biotechnology companies are extremely volatile, and experience fluctuations that are often unrelated or disproportionate to the operating performance of these companies. These broad and sector- specific market fluctuations can result in extreme fluctuations in the price of our ordinary shares, regardless of our operating performance, and can cause our shareholders to lose some or all of their investment in us. We issued pre- funded warrants as part of our June 2022 financing, which may cause additional dilution to our shareholders. In June 2022, we closed an underwritten offering in which we issued and sold 25, 464, 483 ordinary shares and, to RA Capital Management, L. P. in lieu of additional ordinary shares, pre- funded warrants (" Pre- Funded Warrants ") to purchase up to 7, 093, 656 ordinary shares at an exercise price of $ 0. 0001 per share. The Pre- Funded Warrants contain a so- called " blocker " provision which provides that they are only exercisable upon receipt of shareholder approval or if such exercise would not cause the aggregate number of ordinary shares or the combined voting power of total securities, in each case, beneficially owned by the holder (together with its affiliates) to exceed 19. 99 % of the number of ordinary shares or total securities, respectively, outstanding immediately after giving effect to the exercise. To the extent the Pre- Funded Warrants above are exercised, additional ordinary shares will be issued and such issuance would dilute existing shareholders and increase the number of shares eligible for resale in the public market. Our principal shareholders and management own a significant percentage of our ordinary shares and will be able to exert significant control over matters subject to shareholder approval. Based on information publicly available to us as of December 31, ~~2022~~ **2023** , our executive officers, our directors and their respective affiliates, and our other significant shareholders beneficially own a significant portion of our outstanding ordinary shares. As a result, these shareholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring shareholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these shareholders may not be the same as or may even conflict with the interests of our other shareholders. For example, these shareholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other shareholders, which could deprive shareholders of an opportunity to receive a premium for their ordinary shares as part of a sale of our company or our assets and might affect the prevailing market price of our ordinary shares. The significant concentration of share ownership may adversely affect the trading price of our ordinary shares due to investors' perception that conflicts of interest may exist or arise. We incur significant costs due to operating as a public company, and our management is required to devote substantial time to compliance initiatives. As a public company, we incur significant legal, accounting and other expenses. We are subject to the reporting and other requirements of the Exchange Act, the Sarbanes- Oxley Act of 2002 (the " Sarbanes- Oxley Act "), and the Dodd- Frank Wall Street Reform and Protection Act, as well as rules subsequently adopted by the SEC and the Nasdaq Stock Market. These rules and regulations require, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition and establish and maintain effective disclosure and financial controls and corporate governance practices. We expect that compliance with these rules and regulations will continue to result in substantial legal and financial compliance costs and will make some activities more time- consuming and costly. Our management and other personnel devote a substantial amount of time to these compliance requirements. If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us. We are required to comply with Section 404 of the Sarbanes- Oxley Act. Section 404 of the Sarbanes- Oxley Act requires public companies to maintain effective internal control over financial reporting. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting. Ensuring that we have adequate internal financial and

accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time- consuming effort that is evaluated frequently. If we fail to maintain the effectiveness of our internal controls or fail to comply in a timely manner with the requirements of the Sarbanes- Oxley Act, or if we identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, this could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our ordinary shares and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would require additional financial and management resources. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. The estimates and judgments we make, or the assumptions on which we rely, in preparing our consolidated financial statements could prove inaccurate. Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States (" U. S. GAAP "). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure, however, that our estimates, or the assumptions underlying them, will not change over time or otherwise prove inaccurate. For example, our estimates as they relate to anticipated timelines and milestones for our clinical trials or preclinical development may prove to be inaccurate. If this is the case, we may be required to restate our consolidated financial statements, which could, in turn, subject us to securities class action litigation. Defending against such potential litigation relating to a restatement of our consolidated financial statements or otherwise would be expensive and would require significant attention and resources of our management. Moreover, our insurance to cover our obligations with respect to the ultimate resolution of any such litigation may be inadequate. As a result of these factors, any such potential litigation could have a material adverse effect on our financial results, harm our business, and cause our share price to decline. We do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. We have never declared or paid cash dividends on our ordinary shares. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business, and we do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our ordinary shares will be our shareholders' sole source of gain for the foreseeable future. We may incur significant costs from class action litigation due to share volatility. Our share price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of our collaborators and / or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. Holders of stock that has experienced significant price and trading volatility have occasionally brought securities class action litigation against the companies that issued the stock. If any of our shareholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management, which could harm our business. Sales of additional ordinary shares could cause the price of our ordinary shares to decline. Sales of substantial amounts of our ordinary shares in the public market, or the availability of such shares for sale, by us or others, including the issuance of ordinary shares upon exercise of outstanding options or Pre- Funded Warrants or vesting of outstanding restricted share units, or the perception that such sales could occur, could adversely affect the price of our ordinary shares. Certain of our shareholders have required us, or have the right to require us, to register the sales of their shares under the Securities Act under agreements between us and such shareholders. For example, in August 2019, we filed a registration statement on Form S- 3, which was declared effective on August 14, 2019, to register the resale from time to time by certain of our executive officers, directors and their affiliates of up to approximately 7. 1 million ordinary shares. If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline. The trading market for our ordinary shares may depend in part on the research and reports that securities or industry analysts publish about us or our business. If too few securities or industry analysts cover our company, the trading price for our ordinary shares would likely be negatively impacted. If one or more of the analysts who cover us downgrade our ordinary shares or publish inaccurate or unfavorable research about our business, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline. 97