Risk Factors Comparison 2025-02-24 to 2024-03-06 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should carefully read and consider all of the risks described below, as well as the other information in this 10- K, including our financial statements and the related notes and the section titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " and in other documents we file with the SEC when evaluating our business. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. Unless otherwise indicated, references to our business being harmed in these risk factors will include harm to our business, reputation, financial condition, results of operations and future prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. The risks described below are not intended to be exhaustive and are not the only risks that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock. Risks Related to Our Financial Position and Need for Additional Capital We have incurred significant losses since our inception, have no products approved for sale and we expect to incur losses for the foreseeable future. Since inception, we have incurred significant operating losses. Our net losses were $ **90. 0 million and $** 78. 6 ~~million and $ 69. 1~~ million for the years ended December 31, ~~2023~~ **2024** and December 31, ~~2022~~ **2023** , respectively. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~181~~ **271** . 5 million. To date, we have financed our operations primarily with the proceeds raised from the sale of our convertible preferred stock in private placements and common stock in our IPO and our equity offerings in early 2024, described below. We have devoted substantially all of our financial resources and efforts to research and development activities, business planning, establishing and maintaining our intellectual property portfolio, acquiring and developing product and technology rights, hiring personnel, leasing premises and associated capital expenditures, raising capital, and providing general and administrative support for these operations. We are still in the early stages of development of our programs and have only advanced two product candidates into clinical development. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we: • **continue to advance** ~~complete preclinical activities for~~ our programs in DMD and DM1 ~~and continue to advance them into and~~ through clinical development **and work to resolve the U. S. clinical hold on the initiation in the U. S. of the CONNECT1 Phase 2 study of PGN- EDO51 in DMD** ; • advance any additional product candidates we identify through our research programs into IND- or CTA- enabling studies and clinical trials following regulatory clearance to commence clinical research; • continue to develop and expand the capabilities of our proprietary EDO platform; • establish manufacturing sources for our product candidates and secure supply chain capacity to provide sufficient quantities for preclinical and clinical development and commercial supply; • seek marketing approvals for any product candidates that successfully complete pivotal clinical trials; • obtain, expand, maintain, defend and enforce our intellectual property portfolio; • hire additional clinical, regulatory and scientific personnel; • ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and • add operational, legal, compliance, financial and management information systems and personnel to support our research, product development and future commercialization efforts, as well as to support our operations as a public company. Even if we obtain regulatory approval of, and are successful in commercializing, one or more of our product candidates, we will continue to incur substantial research and development and other costs to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. We have never generated revenue from product sales and may never achieve or maintain profitability. While we have completed our Phase 1 clinical trial for PGN- EDO51 and initiated ~~a~~ **two** Phase 2 clinical ~~trial~~ **trials** for PGN- EDO51 **as well as** ~~and~~ **an** ~~our~~ **additional** Phase 1 clinical trial for PGN- EDODM1 **and more recently, a Phase 2 clinical trial for PGN- EDODM1** , we expect that it will be many years, if ever, before we have a product candidate ready for commercialization. **In December 2024, the FDA issued a clinical hold on the initiation of our Phase 2 CONNECT2 trial of PGN- EDO51 in DMD in the U. S. It is unknown whether we may be successful in resolving this hold. More recently, Health Canada has requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 study of PGN- EDO51. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study. Moreover, even if we are successful in removing the FDA clinical hold, it is unknown whether the FDA may require the conduct of additional preclinical studies or clinical trials beyond those which we had planned to conduct.** To become and remain profitable, we must succeed in developing, obtaining the necessary regulatory approvals for and eventually commercializing a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including: • identifying product candidates and completing preclinical development of our product candidates; • obtaining regulatory ~~authorization~~ **clearance** to commence clinical trials and initiating and successfully completing such trials; • obtaining marketing approval for our product candidates; • manufacturing (or securing third- party manufacturers to manufacture), marketing and selling any products for which we may obtain regulatory approval; • achieving market acceptance of any products for which we obtain regulatory approval as a viable treatment option; and • satisfying any post- marketing requirements. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and,

even if we do, may never generate revenues that are significant enough to achieve profitability ~~. We completed a Phase 1 clinical trial for our first product candidate, PGN- EDO51 and initiated a Phase 2 clinical trial for PGN- EDO51 as well as a Phase 1 clinical trial for PGN- EDODM1~~ . Because of the numerous risks and uncertainties associated with product development, we are unable to accurately estimate or know the nature, timing or costs of the efforts that will be necessary to complete the preclinical and clinical development and commercialization of our product candidates or when, or if, we will be able to generate revenues or achieve profitability. If we are successful in obtaining regulatory approval to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. 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 could impair our ability to raise capital, maintain our research and development efforts, expand our business or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment. We will need to raise substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, scale back or discontinue our product development programs or future commercialization efforts. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we identify, continue the research and development of, continue preclinical testing and initiate clinical trials of, arrange for the manufacturing of, and potentially seek marketing approval for any product candidates that successfully completes clinical testing. To date, we have only completed a Phase 1 clinical trial for our first product candidate, PGN- EDO51 ~~and~~ **,** initiated **one additional Phase 1 clinical trial for PGN- EDODM1, two** Phase 2 clinical trials for PGN- EDO51 ~~as well as a~~ **and more recently, one** Phase ~~1~~ **2** clinical trial for ~~our second product candidate,~~ PGN- EDODM1 **. The resolution of the clinical hold in the U. S. on the initiation of the Phase 2 CONNECT2 clinical trial of PGN- EDO51, assuming resolution is reached with the FDA, may require additional capital beyond that we had planned to allocate to this program, and the amount of such capital could be considerable** . In addition, if we obtain marketing approval for any product candidate, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed, on attractive terms or at all, we may be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. As of December 31, ~~2023~~ **2024** , we had cash, cash equivalents, and marketable securities of $ ~~110~~ **120** . ~~4~~ **2** million. ~~In July~~ **Prior to our IPO in May** ~~2021~~ **2022** , we raised aggregate gross proceeds of $ ~~21~~ **133** . ~~0~~ **5** million from the **private placement** ~~final milestone closing~~ of ~~our Series A- 2~~ convertible preferred stock ~~and aggregate gross proceeds of $ 112~~ . **We** ~~5 million from the private placement of our Series B convertible preferred stock. In addition, in May 2022, we~~ raised aggregate gross proceeds of $ 122. 9 million from our IPO. On February 5, 2024, we sold shares **of common stock** under our at- the- market offering program, or ATM program, pursuant to an At- the- Market Equity Offering Sales Agreement, or Sales Agreement, with Stifel, Nicolaus & Company, Incorporated, **or Stifel,** resulting in net proceeds of $ 9. 9 million **.** . On February 9, 2024, we sold shares **of common stock** in ~~a~~ **an underwritten** follow- on offering, or the Follow- on Offering, resulting in net proceeds of $ 76. ~~9~~ **4** million after deducting underwriters' fees of $ 3. ~~2~~ **7** million. Net proceeds from the ATM program and Follow- on Offering, after deducting underwriters' fees and ~~before deducting~~ costs of the offerings, were $ 86. ~~8~~ **3** million. Based on our ~~current~~ **currently planned** ~~operating~~ **operations** ~~plans~~ , we believe that our existing cash, cash equivalents, marketable securities ~~, including proceeds from shares sold under our ATM program and in the Follow- on Offering,~~ will be sufficient to fund our operations ~~into 2026~~ **for at least 12 months from the date of the filing of this 10- K** . However, we have based this estimate on assumptions that may prove to be wrong, and our operating plans may change as a result of many factors, including factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect and could be forced to seek additional funding sooner than planned. Our future capital requirements will depend on many factors, including: • the scope, progress, costs and results of preclinical and clinical development for our product candidates and any additional product candidates we may develop or any new indications we may pursue; • the scope, costs, timing and outcome of regulatory review of our product candidates and any additional product candidates we may develop or any new indications we may pursue; • the cost and timing of manufacturing activities; • the identification of additional research programs and product candidates; • the costs and scope of the continued development of our EDO platform; • the costs and timing of preparing, filing and prosecuting applications for patents, maintaining and enforcing our intellectual property rights and defending any intellectual property- related claims, including claims of infringement, misappropriation or other violations of third- party intellectual property; • the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidate that receives marketing approval; • the costs of satisfying any post- marketing requirements; • the revenue, if any, received from commercial sales of our product candidates if marketing approval is received; • the costs of operational, financial and management information systems and associated personnel; • the associated costs in connection with any acquisition of in- licensed products, intellectual property and technologies; and • the costs of operating as a public company. Identifying potential product candidates and conducting preclinical testing and clinical trials **are** ~~is a~~ time- consuming, expensive and uncertain ~~process~~ **processes requiring** ~~that takes~~ years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, may not be sufficient to sustain our operations. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be

available to us on acceptable terms, or at all. Any additional fundraising efforts may divert our management from their day- to-day activities, which may adversely affect our operations. We cannot be certain that additional funding will be available on acceptable terms, when needed or at all. We have no committed source of additional capital and, if we are unable to raise additional capital in sufficient amounts, when needed or on terms acceptable to us, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline. Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability. We commenced operations in 2018, have no products approved for commercial sale and have not generated any revenue from product sales. To date, our operations have been limited to organizing and staffing our company, business planning, executing collaborations, raising capital, licensing, conducting research activities, conducting preclinical studies of our programs and clinical trials of our product candidates, filing and prosecuting patent applications and providing general and administrative support for these operations. One of our product candidates, PGN- EDO51, completed a Phase 1 clinical trial and we have initiated **one additional** ~~Phase 2 clinical trials of PGN- EDO51 in DMD patients amenable to exon 51 skipping, as well as a~~ Phase 1 clinical trial for ~~another product candidate,~~ PGN- EDODM1 **and two Phase 2 clinical trials for PGN- EDO51 and more recently** , **a Phase 2 clinical trial for PGN- EDODM1. In December 2024, the FDA issued a clinical hold on the initiation of our Phase 2 CONNECT2 trial of PGN- EDO51** in ~~DM1 patients~~ **DMD in the U. S. It is unknown whether we may be successful in resolving this hold. Moreover, even if we are successful in removing the hold, it is unknown whether the FDA may require the conduct of additional preclinical studies or clinical trials beyond those which we had planned to conduct. More recently, Health Canada has requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 Phase 2 study of PGN- EDO51 in DMD. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study** . All of our other research programs are still in the research or preclinical stage of development, and their risk of failure is high. We have not yet demonstrated our ability to successfully complete clinical trials consistently, obtain marketing approvals, manufacture product on a commercial scale or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make 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 products ~~.~~ Our limited operating history may make it difficult to evaluate our technology and industry and predict our future performance. Our limited history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early- stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer. In addition, as our business grows, we may encounter unforeseen expenses, restrictions, difficulties, complications, delays and other known and unknown factors. We will need to continue to transition from a company with a research focus to a company capable of conducting development activities for multiple product candidates and then to a company supporting commercial activities. We may not be successful in such transitions. If we do not adequately address these risks and difficulties or successfully make such a transition, it could have a material adverse impact on our business. Risks Related to Discovery, Development, Preclinical and Clinical Testing We are early in our development efforts. We have only completed a Phase 1 clinical trial for our lead product candidate and initiated **several additional** ~~a Phase 1 clinical trial of a second product candidate as well as Phase 2~~ clinical trials ~~of our lead product candidate~~ , and as a result it will be years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed. We are early in our development efforts and have invested our research efforts to date in developing our EDO platform. We have a portfolio of research programs **,** and we have two product candidates in clinical trials — PGN- EDO51 for DMD and PGN- EDODM1 for DM1. We have completed a Phase 1 clinical trial for our first product candidate, PGN- EDO51 **in HVs** . We have initiated our Phase 2 CONNECT1 trial for PGN- EDO51 in Canada ~~,~~ and began dosing ~~patients~~ **participants** in January of 2024 **. In July 2024, we reported initial data from the low dose cohort (5 mg / kg) in this trial. Based on this data, we have amended the CONNECT1 study protocol to implement several changes. Following notification of the FDA clinical hold referenced below, Health Canada requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 study. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study** . We received clearance from the MHRA to initiate our ~~multinational~~ Phase 2 CONNECT2 trial for PGN- EDO51 in ~~February~~ **the U. K. In December** 2024 **, the FDA issued a clinical hold on the initiation of the CONNECT2 clinical trial in the U. S** . We have initiated a Phase 1 clinical trial, designated FREEDOM, for our second product candidate, PGN- EDODM1, and began dosing ~~patients~~ **participants** in December 2023. **On February 24, 2025, we reported initial single- dose data for each of the first two cohorts (5 and 10 mg / kg) in the Phase 1 FREEDOM study.** We **have also opened a Phase 2 clinical trial, FREEDOM2, in Canada and the U. K. We are evaluating additional product candidates in preclinical studies, but** have not completed IND- or CTA- enabling activities for any of our other product candidates or advanced any of our other product candidates into clinical trials. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful

clinical development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product. Commencing clinical trials in the U. S. is subject to authorization by the FDA ~~,~~ of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies **,** or we are required to satisfy other FDA or other regulator requests prior to commencing clinical trials, the start of our clinical trials may be delayed. ~~For example~~ **As noted above, in December 2024, we announced that FDA had placed a clinical hold on the initiation of our planned Phase 2 CONNECT2 trial in the U. S. In addition, previously** , in May 2023, we announced that FDA had placed a clinical hold on our planned Phase 1 FREEDOM clinical trial of PGN- EDODM1 in the U. S. We submitted a response to the FDA and in October 2023, we announced that the FDA had lifted the clinical hold, allowing us to initiate FREEDOM in the U. S. Even after initiating FREEDOM in the U. S., the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial, including ~~with respect to~~ **our FREEDOM2 study of** PGN- EDODM1, **or disagree with** or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to CTAs in other countries, including Canada and countries in Europe **. Moreover, regulatory authorities in other countries could request that we pause dosing or further enrollment in one or more of our ongoing studies based in whole or in part on a clinical hold in the U. S** . Commercialization of our product candidates will require preclinical and clinical development; regulatory approval; manufacturing supply, capacity and expertise; a commercial organization; and significant marketing efforts. The success of our product candidates will depend on many factors, including the following: • timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable; • regulatory ~~authorization~~ **clearance** to initiate clinical trials under INDs, CTAs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for our product candidates; • successful initiation, enrollment and completion of clinical trials, including under the FDA' s ~~GCPs~~ **GCP** , ~~GLPs~~ **GLP** , and any additional regulatory requirements from foreign regulatory authorities; • positive results from our clinical trials that support a finding of safety and effectiveness and an acceptable risk- benefit profile in the intended populations to the satisfaction of the applicable regulatory authorities; • receipt of marketing approvals from applicable regulatory authorities, including the completion of any required post- marketing studies or trials; • establishment of arrangements through our own facilities or with third- party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities; • establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for our product candidates; • commercial launch of our product candidates, if approved, whether alone or in collaboration with others; • acceptance of the benefits and use of our product candidates, including method of administration, if and when approved, by patients, the medical community and third- party payors; • effective competition with other therapies; • maintenance of a continued acceptable safety, tolerability and efficacy profile of our product candidates following marketing approval, including acceptable results from any post- approval studies or clinical trials agreed to by us or required by FDA or other regulatory authorities; and • establishment and maintenance of healthcare coverage and adequate reimbursement by payors. Many of these factors are beyond our control and if we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates, which would materially harm our business. If we are unable to advance our product candidates to clinical development or successfully complete clinical trials, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed. Our approach to the discovery and development of product candidates based on our EDO platform is unproven, and we may not be successful in our efforts to identify, discover or develop potential product candidates. The success of our business depends upon our ability to identify, develop and commercialize products based on our proprietary EDO platform. Our current product candidates that have been developed through our EDO platform are peptide- conjugated oligonucleotides designed to have a disease- modifying impact on degenerative neuromuscular diseases. Our lead product candidates are currently in clinical- stage development, while our other product candidates are still in the research or preclinical stage of development and our approach to treating muscle disease is unproven. Our research programs may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates and our potential product candidates may be shown to have harmful side effects in preclinical in vitro experiments or in vivo animal model studies, or in future clinical studies. In addition, our potential product candidates may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture, unmarketable or unlikely to receive marketing approval. Further, because all of our development programs are based on our EDO platform, adverse developments with respect to one of our programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other programs. **In addition, we may be negatively impacted by the decision of other companies to discontinue development of products using technology similar to our technology. For example, recently, Sarepta announced that it was discontinuing its SRP- 5051 peptide- linked PMO development program, based on the risk- benefit of the program, including some patients experiencing hypomagnesemia even after treatment with SRP- 5051 was discontinued, feedback from the FDA, and the evolving therapeutic landscape for DMD.** We have advanced our first two product candidates, PGN- EDO51 and PGN- EDODM1, into the clinic, and have completed a Phase 1 trial of PGN- EDO51 in HVs. However, the positive results we have observed in our preclinical studies and in the completed Phase 1 trial may not be repeated in future clinical trials, including in patients with DMD amenable to ~~a DMD~~ **an exon- 51** skipping approach, and regulatory authorities may disagree with the interpretation of data from our trials. Although we are advancing our initial programs in DMD and DM1, our EDO platform may fail to yield additional product candidates for clinical

development for a number of reasons, including those discussed in these risk factors. In addition: • we may not be able to assemble sufficient resources to acquire or discover product candidates; • competitors may develop alternatives that render our potential product candidates obsolete or less attractive; • potential product candidates we develop may be covered by third parties' patents or other intellectual property rights; • potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance; • potential product candidates may not be effective in treating their targeted diseases or disorders; • the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable; • a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; **or** • the regulatory pathway for a potential product candidate may be too complex and difficult to navigate successfully or economically. If we are unable to identify and discover suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations. Drug development is a lengthy and expensive process, and preclinical and clinical testing is uncertain as to the outcome. We may encounter substantial delays in the commencement, enrollment or completion of our clinical trials and may never advance to clinical trials, or we may fail to demonstrate safety and effectiveness to the satisfaction of applicable regulatory authorities, which could prevent us from advancing or commercializing our product candidates on a timely basis, if at all. The risk of failure in developing product candidates is high. It is impossible to predict when or if any product candidate would prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development, obtain regulatory ~~authorization~~ **clearance** to commence clinical trials, and then conduct extensive clinical trials to demonstrate the safety and efficacy of product candidates in humans. To date, we have only completed a Phase 1 clinical trial of PGN- EDO51 and initiated ~~a~~ **an additional** Phase 1 clinical trial of PGN- EDODM1 ~~and~~ **, two** Phase 2 clinical trials of PGN- EDO51 **and more recently, a Phase 2 clinical trial of PGN- EDODM1** . Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses, and earlier results, both preclinical and clinical, may not be indicative of future clinical trial results. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance, varying interpretations of clinical data or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support clearance of our INDs, CTAs and other similar regulatory filings. We cannot be certain if the outcome of our preclinical studies and clinical trials will ultimately support further development of our product candidates or future programs **, or future regulatory approval and commercialization** . Although we have completed a Phase 1 study of our lead product candidate, PGN- EDO51, ~~and~~ initiated ~~a~~ **two Phase 2 studies of PGN- EDO51 and initiated an additional** Phase 1 **and a Phase 2** clinical trial of our second candidate, PGN- EDODM1, we cannot be certain of the completion or outcome of our preclinical testing and studies for our other product candidates and cannot predict whether the FDA, **European Medicines Agency, or** EMA **,** or comparable foreign regulatory authorities will accept our proposed clinical programs **for PGN- EDO51 or PGN- EDODM1,** or whether the outcome of our preclinical testing and studies will ultimately support the further development of our other product candidates **. For example, Health Canada has recently requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our Phase 2 CONNECT1 study of PGN- EDO51 in DMD. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study. In addition, in December 2024, the FDA issued a clinical hold on the initiation of our Phase 2 CONNECT2 trial of PGN- EDO51 in DMD planned to be initiated in the U. S. It is unknown whether we may be successful in resolving this hold. Moreover, even if we are successful in removing the hold, it is unknown whether the FDA may require the conduct of additional preclinical studies or clinical trials beyond those which we are conducting or plan to conduct** . Conducting preclinical testing is a lengthy, time- consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. In addition, the progress and timing of our preclinical studies, including pharmacology and toxicology studies, may be impacted by the limited supply of NHPs needed for such studies. As a result, we cannot be sure that we will be able to submit INDs, CTAs and other similar regulatory filings for our ~~preclinical~~ programs on the timelines we expect, if at all, and we cannot be sure that submission of such regulatory filings will result in the FDA, EMA or comparable foreign regulatory authorities allowing clinical trials to begin **, including in the case of our CONNECT2 clinical study for PGN- EDO51 and our FREEDOM2 clinical study for PGN- EDODM1** . For example, in May 2023, we announced that we received a clinical hold notice from the FDA regarding our IND application to initiate our Phase 1 FREEDOM study, and in June 2023, we provided an update on our plans with respect to this program. In October 2023, we announced that the FDA lifted the clinical hold on our Phase 1 FREEDOM study, allowing this study to proceed in the U. S. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of **,** or enrollment in clinical trials and could impact our ability to continue to conduct our clinical trials. Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. Other events that may prevent successful or timely completion of clinical development include: • delays in reaching a consensus with regulatory authorities on trial design; • delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites; • delays in opening clinical trial sites or obtaining required IRB **,** or independent ethics committee approval, or

the equivalent review groups for sites outside the U. S., at each clinical trial site; • imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or manufacturing concerns or after an inspection of our clinical trial operations or trial sites; • negative or inconclusive results observed in clinical trials, including failure to demonstrate statistical significance, which could lead us, or cause regulators to require us, to conduct additional clinical trials or abandon product development programs; • failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements; • failure to perform in accordance with the FDA' s GCPs or those of other regulatory authorities; • failure by physicians to adhere to delivery protocols leading to variable results; • delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions; • failure of our third- party contractors to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all; • inability to recruit patients to participate in a clinical trial, including as a result of competition with other pharmaceutical and biotechnology companies and the patient population size for our product candidates; • delays in having patients complete participation in a clinical trial or return for post- treatment follow- up; • clinical trial sites or patients dropping out of a trial; • selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data; • occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; • occurrence of serious adverse events associated with a product candidate in development by another company, which are viewed to outweigh its potential benefits, and which may negatively impact the perception of our product due to a similarity in technology or approach; • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; • changes in the legal or regulatory regimes domestically or internationally related to patient rights and privacy; • lack of adequate funding to continue the clinical trial; or • lack of diminished revenue potential of the program (s) due to competition. Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and IRBs or ethics committees at the medical institutions where the clinical trials are conducted. We could encounter delays if a clinical trial is suspended or terminated by us, by the **DSMB** ~~data safety monitoring board~~ for such trial or by the FDA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, disruptions caused by the effects of ~~the COVID- 19 pandemic, or~~ any ~~future~~ **epidemics or** pandemics ~~,~~ may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our product candidates. Any inability to successfully complete preclinical studies and clinical trials could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects. Further, conducting clinical trials in foreign countries, as we plan to continue to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Additionally, if the results of clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may: • be delayed in obtaining marketing approval for product candidates, if at all; • obtain approval for indications or patient populations that are not as broad as intended or desired; • obtain approval with labeling that includes significant use or distribution restrictions or safety warnings; • be subject to changes in the way the product is administered; • be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; • have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a REMS; • be subject to the addition of labeling statements, such as warnings or contraindications; • be sued; or • experience damage to our reputation. In particular, each of the conditions for which we plan to develop **or are developing** product candidates ~~are~~ **is a** rare genetic ~~diseases~~ **disease** with limited patient pools from which to draw for clinical trials. Further, because it can be difficult to diagnose these diseases in the absence of a genetic screen, we may have difficulty finding patients who are eligible to participate in our studies. The eligibility criteria of our clinical trials will further limit the pool of available study participants. Additionally, the process of finding and diagnosing patients may prove costly. The treating physicians in our clinical trials may also use their medical discretion in advising patients enrolled in our clinical trials to withdraw from our studies or to try alternative therapies.

Finally, we must compete with other companies with either approved therapies or investigational therapies in development for the conditions which we are developing product candidates for, which may further limit the pool of potential patients. The outcome of preclinical studies and earlier- stage clinical trials may not be predictive of future results or the success of later preclinical studies and clinical trials. We are in the early stages of our programs and have successfully completed a Phase 1 **HV** clinical trial in Canada for our lead product candidate, PGN- EDO51, ~~and have~~ **reported early data from the low dose cohort of our first Phase 2 trial of PGN- EDO51 in DMD patients,** initiated ~~a~~ Phase 1 **and Phase 2** clinical ~~trial~~ **trials** for our PGN- EDODM1 product candidate **and reported initial data from the first two cohorts of our Phase 1 trial of PGN- EDODM1** , but we have not completed IND- or CTA- enabling activities for our other product candidates or advanced any other product candidates into clinical development. As a result, our belief in the capabilities of our platform is based on early research, preclinical studies ~~and~~ **,** our completed Phase 1 clinical trial in HVs **and early data from our Phase 2 study of PGN- EDO51 and our Phase 1 study of PGN- EDODM1** . However, the results of preclinical studies may not be predictive of the results of later preclinical studies or clinical trials, and the results of any early- stage clinical trials may not be predictive of the results of later clinical trials. For example, we may not see the same levels of exon skipping, oligonucleotide delivery or dystrophin production in DMD patients as was observed in our preclinical studies or, with respect to exon skipping **and oligonucleotide delivery** , in our Phase 1 HV study of PGN- EDO51. **While we saw high mean levels of exon skipping (2. 15 %) in all participants at the 5 mg / kg starting dose of our CONNECT1 Phase 2 study after four doses and three months of treatment, we did not achieve the level of dystrophin that we had anticipated. With a longer treatment period and higher doses of PGN- EDO51, we expect to see higher levels of exon skipped transcript potentially resulting in significant increases in dystrophin, but this may not be the case. Given Health Canada' s recent request for additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 study, we may be unable to further advance the CONNECT1 study beyond dosing of the currently enrolled participants at current dose levels.** In addition, **with the current clinical hold on initiation of our CONNECT2 clinical trial in the U. S. for PGN- EDO51 in DMD, we may be unable to advance development of PGN- EDO51 for DMD in the U. S. On February 24, 2025, we reported** initial **single- dose data for each of the first two cohorts (5 and 10 mg / kg) in the Phase 1 FREEDOM study. While we observed robust and dose- dependent mean splicing correction (29. 1 %) at the 10 mg / kg dose level, we observed limited change in functional outcomes after a single dose over one month. We believe robust splicing correction with PGN- EDODM1 has the potential to lead to meaningful functional improvements with repeat dosing over time, but this may not be the case. Initial** success in clinical trials **, including in our CONNECT1 and FREEDOM studies,** may not be indicative of results obtained when such trials are completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our clinical trials may not ultimately be successful or support further clinical development of our product candidates. There is a high failure rate for product candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business and results of operations. Additionally, our planned clinical trials may utilize an " open- label " trial design. An " open- label " clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open- label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open- label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open- label clinical trials are aware when they are receiving treatment. Open- label clinical trials may be subject to a " patient bias " where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open- label clinical trials may be subject to an " investigator bias " where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open- label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a controlled environment with a placebo or active control. If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to complete clinical trials may be adversely impacted. Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment and trial completion is affected by factors including: • perceived risks and benefits of novel unproven approaches; • size of the patient population, in particular for rare diseases such as the diseases on which we are initially focused, and process for identifying patients; • design of the trial protocol; • eligibility and exclusion criteria; • perceived risks and benefits of the product candidate under study; • availability of competing therapies and clinical trials; • severity of the disease or disorder under investigation; • proximity and availability of clinical trial sites for prospective patients; • ability to obtain and maintain patient consent; • risk that enrolled patients will drop out before completion of the trial; • ability to recruit clinical trial investigators of appropriate competencies and experience; • patient referral practices of physicians; • ability to monitor patients adequately during and after treatment; and • other factors outside of our control, such as the potential effects of **any epidemics,** ~~the COVID- 19 pandemic~~ **pandemics** ~~or a future pandemic~~ or health crisis. **For example, DMD amenable to exon 51 skipping is a rare disease, and there are several therapies approved in certain territories or in clinical development, which can make enrollment in our CONNECT1 and CONNECT2 trials more challenging.** Our inability to enroll a sufficient number of patients for **our** clinical trials **, including our ongoing trials for PGN- EDO51 and PGN- EDODM1,** would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased

development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we rely on and expect to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance. Even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining patients in our clinical trials. Many of the patients who end up receiving placebo may perceive that they are not receiving the product candidate being tested, and they may decide to withdraw from our clinical trials to pursue other alternative therapies rather than continue the trial with the perception that they are receiving placebo. If we have difficulty enrolling or maintaining a sufficient number of patients to conduct our clinical trials, we may need to delay, limit or terminate clinical trials, any of which would harm our business, financial condition, results of operations and prospects. Interim, initial, " topline ", and preliminary data from our preclinical studies or clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. For example, in September 2022, we announced results from our Phase 1 clinical trial of PGN- EDO51 **, in July 2024, we announced initial results from our CONNECT1 Phase 2 trial from the low dose (5 mg / kg) cohort as well as high level safety information for the ongoing 10 mg / kg dose cohort, and more recently, we provided additional safety information from the ongoing CONNECT1 trial. On February 24, 2025, we announced initial results from our FREEDOM Phase 1 trial from the 5 and 10 mg / kg dose cohorts** . The topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data and preliminary results should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data could result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. If any of our product candidates cause undesirable side effects or have other unexpected adverse properties, such side effects or properties could delay or prevent the initiation or completion of clinical trials, regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval. **We** ~~While we~~ have ~~only~~ completed dosing up to 15 mg / kg in a Phase 1 clinical trial of PGN- EDO51, in which PGN- EDO51 was **observed to be** generally well- tolerated **in HVs** at clinically active doses, **and are dosing participants at 5 mg / kg and 10 mg / kg in an ongoing Phase 2 clinical trial of PGN- EDO51, in which we believe PGN- EDO51 has continued to demonstrate a favorable safety profile as of January 23, 2025, but** there can be no assurance that our product candidates will not cause undesirable side effects in patients. For example, in preclinical toxicology studies of PGN- EDO51 in normal NHPs, we observed transient, clinical signs of hypotension in some animals treated at a dose level higher than that which we intend to evaluate in the clinic. In addition, in our Phase 1 clinical trial of PGN- EDO51, at 15 mg / kg, we observed mild, transient, reversible changes in kidney biomarkers that resolved without intervention in all but one participant who experienced a non- life threatening serious adverse event. While the trial was not halted by the safety review committee nor put on hold by Health Canada, under the protocol for this Phase 1 clinical trial, any non- life- threatening SAE was considered a **DLT** ~~dose- limiting toxicity~~ . This participant was admitted to the hospital for less than 24 hours, received intravenous hydration, and then was re-admitted to the Phase 1 unit and completed the study. We also observed transient mild to moderate hypomagnesemia in two participants in the Phase 1 trial, which did not require intervention. Based on published data and other publicly available information, such adverse events are consistent with the types of events reported with this class of oligonucleotides in general **. In the ongoing CONNECT1 Phase 2 study, based on the totality of data in both the 5 mg / kg cohort and the ongoing 10 mg / kg cohort as of January 23, 3025, we continue to believe PGN- EDO51 has a favorable emerging safety profile. Magnesium levels in two of the participants in the 10 mg / kg cohort, who were previously reported as having asymptomatic hypomagnesemia, have returned to levels within normal limits with administration of ongoing low- dose oral magnesium supplementation. Dosing of one of these two participants was paused due to a reduction of his eGFR. This event did not meet the pre- specified criteria for a DLT. A subsequent nuclear scan indicated measured glomerular filtration rate was in the normal range. The participant' s eGFR is improving and the investigator is evaluating for the resumption of dosing as this value returns to baseline levels. We are continuing to review the event and associated potential confounding factors to better understand its manifestation. There have been no treatment- related SAEs, and all treatment- related adverse events have been mild. There was no sustained elevation in kidney biomarkers. There were also no cases of hypokalemia, anemia or thrombocytopenia. We have received communication from Health Canada**

that dosing of participants in the 5 and 10 mg / kg cohorts may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels. On February 24, 2025, we reported initial data from the 5 and 10 mg / kg dose cohorts in our FREEDOM Phase 1 study in DM1 patients. We believe PGN- EDODM1 has a favorable emerging safety profile. Through the data cutoff date of December 3, 2024, PGN- EDODM1 was observed to be generally well- tolerated, with most TEAEs being mild or moderate in severity. There were no adverse events related to electrolytes or renal biomarkers. There can be no assurance that PGN- EDODM1 will not cause undesirable side effects in patients with further dosing and dose escalation, including safety events similar to those observed in our studies with PGN- EDO51 . Although other oligonucleotide therapeutics have received regulatory approval, ours is a novel approach to oligonucleotide therapy. As a result, there is uncertainty as to the safety profile of our product candidates compared to more well- established classes of therapies, or oligonucleotide therapeutics on their own. Moreover, there have been only a limited number of clinical trials involving the use of peptide conjugated oligonucleotide therapeutics and only one completed trial involving the proprietary technology used in our EDO platform. Despite the outcome of our Phase 1 clinical trial of PGN- EDO51 ~~,~~ **and the early** results **from our Phase 2 CONNECT1 study, as well as the initial results from our Phase 1 clinical trial** of **PGN- EDODM1, further results from our CONNECT1** ~~our~~ **or FREEDOM trials or future results from our CONNECT2** Phase 2 clinical trials for PGN- EDO51 or **our FREEDOM2 Phase 2 clinical trial of PGN- EDODM1, or studies of** any other product candidate could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics than previously anticipated. If any product candidates we develop are associated with serious adverse events, undesirable side effects or unexpected characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, regulatory authorities may draw different conclusions, require additional testing to confirm these determinations, require more restrictive labeling or deny regulatory approval of the product candidate. Many product candidates that initially showed promise in early- stage testing have later been found to cause side effects that prevented further clinical development of the product candidates. It is possible that, as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our product candidates becomes more widespread following any regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly. In addition, if our product candidates receive marketing approval, and we or others later identify undesirable side effects caused by treatment with such drug, a number of potentially significant negative consequences could result, including: • regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution; • we may be required to recall a product or change the way the drug is administered to patients; • regulatory authorities may require additional warnings in the labeling, such as a contraindication or a boxed warning, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product; • we may be required to change the way the product is administered or conduct additional clinical trials or post- approval studies; • we may be required to implement a REMS, or create a medication guide outlining the risks of such side effects for distribution to patients; • additional restrictions may be imposed on the marketing or promotion of the particular product or the manufacturing processes for the product or any component thereof; • we may be subject to fines, injunctions or the imposition of criminal penalties; • we could be sued and held liable for harm caused to patients; • the drug could become less competitive; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of our lead product candidate or our other product candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects. We may expend our limited resources to pursue a particular program, product candidate or indication and fail to capitalize on programs, product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on research programs and expect to focus on product candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential, or we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. 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 medicines. 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 such event could have a material adverse effect on our business, financial condition, results of operations and prospects. The increasing use of social media platforms presents new risks and challenges. Social media is increasingly being used to communicate about pharmaceutical companies' clinical development activities, and we intend to utilize appropriate social media in connection with our development efforts. Additionally, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur in the future in connection with any of our sponsored clinical trials, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public' s legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about

our product candidates. There is also a risk of inappropriate disclosure of sensitive or confidential information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management or our product candidates, and fraudsters could and have attempted to illegally use our name on social media platforms to defraud the public. **It is also possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our product candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed.** If any of these events were to occur or we fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business. Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of our product candidates. We ~~will~~ face an inherent risk of clinical trial and product liability exposure related to the testing of product candidates that **have entered or eventually** proceed to clinical trials, and we will face an even greater risk if we commercially sell any products that receive marketing approval. While we currently have only two product candidates in clinical development and none that have been approved for commercial sale, the future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for our product candidates; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial participants; • significant costs to defend any related litigation; • substantial monetary awards to trial participants or patients; • loss of revenue; • reduced resources of our management to pursue our business strategy; and • the inability to commercialize our product candidates. We have insurance coverage in place that we believe to be appropriate for our current phase of clinical development, but we may need to further increase this coverage for subsequent clinical trials, or if we commence commercialization of any product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired. We intend to conduct certain clinical trials for our product candidates outside of the U. S. However, the FDA and comparable foreign regulatory authorities may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business. We conducted our first clinical trial in Canada, and we intend to conduct one or more of our subsequent clinical trials for our product candidates outside the U. S., including our ongoing CONNECT1 **Phase 2** trial in Canada, and our **ongoing** CONNECT2 **,** ~~trial and~~ FREEDOM **and FREEDOM2** clinical ~~trial~~ **trials** , ~~both~~ **each** of which **has or** will have sites in multiple countries outside of the U. S. Although the FDA may accept data from clinical trials conducted outside the U. S., acceptance of this data is subject to certain conditions imposed by the FDA. Where data from foreign clinical trials are intended to serve as the basis for marketing approval in the U. S., the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the U. S. population and U. S. medical practice; the studies were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on- site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. For studies that are conducted only at sites outside of the U. S. and not subject to an IND, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non- U. S. clinical trial was inadequate, which could require us to conduct additional clinical trials. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well- designed and well- conducted in accordance with GCP and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. There can be no assurance the FDA will accept data from clinical trials conducted outside of the U. S. If the FDA does not accept data from our clinical trials of our product candidates, it would likely result in the need for additional clinical trials, which would be costly and time consuming and delay or permanently halt our development of our product candidates. Conducting clinical trials outside the U. S. also exposes us to additional risks, including risks associated with: • additional foreign regulatory requirements; • foreign exchange fluctuations; • compliance with foreign manufacturing, customs, shipment and storage requirements; • cultural differences in medical practice and clinical research; and • diminished protection of intellectual property in some countries. Risks Related to Our Dependence on Third Parties We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily. We do not expect to independently conduct all aspects of our product manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to many of these items, including ~~contract development manufacturing organizations, or~~ CDMOs, for the manufacturing of any product candidates we test in preclinical or clinical development, as well as CROs for the conduct of our animal testing and research **and** for the conduct of our current and planned clinical trials. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could 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 responsibility to ensure compliance with all required regulations and study protocols. For example, we will remain responsible for ensuring that each of our IND- and CTA- enabling studies and clinical trials are conducted in accordance with the study plan and protocols. Moreover, the FDA requires us to comply with GCPs for 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 trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under conditions that comply with the FDA' s ~~current Good Manufacturing Practices, or~~ cGMPs. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Although we intend to design the preclinical studies and clinical trials for our product candidates, CROs will conduct some or all of the preclinical studies and clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may: • have staffing difficulties; • fail to comply with contractual obligations; • experience regulatory compliance issues; • undergo changes in priorities or become financially distressed; or • form relationships with other entities, some of which may be our competitors. These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If the CROs and other third parties do not perform preclinical studies and clinical trials in a satisfactory manner, if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, or if they breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs and other third parties, we could be required to repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures. If 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 preclinical studies and clinical trials required to support future IND, CTA and other similar regulatory filings and potential approval of our product candidates. In addition, there are few CDMOs ~~who~~ **that** have the capability to ~~both, on the one hand,~~ manufacture oligonucleotides and peptides, ~~and, on the other hand, conjugate them~~ - **the key intermediates in the synthesis of the final active pharmaceutical ingredient** , both of which ~~processes~~ are critical to the development and production of our product candidates. We are aware that one or more **of our** competitors **are using either oligonucleotides, peptides, or both in their product candidates, and that they** have engaged **with** many of these CDMOs, which may hinder our ability to also contract with those CDMOs. As a result, we may have difficulty finding and engaging sufficient third- party manufacturers to develop and manufacture our product candidates, which may affect our ability to conduct preclinical studies and clinical trials **. Moreover, legislative proposals are pending that, if enacted, could negatively impact U. S. funding for certain biotechnology providers, including some of our vendors, that may have relationships with certain foreign governments or are viewed as posing a threat to national security. If certain of these vendors are unable to continue to provide services or we are unable to contract with such vendors, this could further constrain our ability to find and engage third- party manufacturers to develop and manufacture our product candidates, which could adversely affect our business** . We currently depend on a small number of third- party suppliers to supply the product candidates that we are evaluating in our research programs. The loss of these or future third- party suppliers, or their inability to provide us with sufficient supply, could harm our business. We do not own or operate manufacturing facilities and have no current plans to develop our own clinical or commercial- scale manufacturing capabilities. We rely on a small number of third- party suppliers for the manufacture of the product candidates that we are evaluating in our research programs. We expect to continue to depend on third- party suppliers for the manufacture of any product candidates we advance into preclinical and clinical development, as well as for commercial manufacture if those product candidates receive marketing approval. The facilities used by third- party manufacturers to manufacture our product candidates must be approved by the FDA, the EMA and any comparable foreign regulatory authority pursuant to inspections that will be conducted after we submit an NDA ~~,~~ to the FDA or any comparable filing to the EMA or other foreign regulatory authority. We do not control the manufacturing process of, and are completely dependent on, third- party manufacturers for compliance with cGMP requirements for the manufacture of products. If these third- party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, the EMA or any comparable foreign regulatory authority, we may incur delays in our clinical trials or regulatory submissions **,** and they will not be able to secure and / or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of third- party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or any comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Our failure, or the failure of our third- party manufacturers, to

comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. We may also seek to eventually establish our own manufacturing facility for the long- term commercial supply of our product candidates for which receive regulatory approval, if any. If we determine to establish our own manufacturing facility and manufacture our products on our own, we will need to obtain the resources and expertise in order to build such manufacturing capabilities and to conduct such manufacturing operations. In addition, our conduct of such manufacturing operations will be subject to the extensive regulations and operational risks to which our third- party suppliers are subject. If we are not successful in building these capabilities or complying with the regulations or otherwise operating our manufacturing function, our commercial supply could be disrupted and our business could be materially harmed. Our or a third party' s failure to execute on our manufacturing requirements on commercially reasonable terms and in compliance with cGMP could adversely affect our business in a number of ways, including: • an inability to initiate or conduct preclinical studies or clinical trials of product candidates; • delays in initiating or completing preclinical studies or clinical trials of product candidates or in submitting regulatory applications, or receiving marketing approvals, for product candidates; • subjecting third- party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities; • requirements to cease development or to recall batches of product candidates; and • in the event of approval to market and commercialize any product, an inability to meet commercial demands for the product. We are party to manufacturing agreements with a number of third- party manufacturers. We may be unable to maintain these agreements or establish any additional agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to maintain or establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: • failure of third- party manufacturers to comply with regulatory requirements and maintain quality assurance; • breach of the manufacturing agreement by the third party; • failure to manufacture according to our specifications; • failure to manufacture according to our schedule or at all; • misappropriation of our proprietary information, including our trade secrets and know- how; and • termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. We ~~may~~ compete with third parties for access to manufacturing facilities **, in particular for the manufacture of oligonucleotides** . There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials. If our existing or future third- party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in supply. An alternative manufacturer would need to be qualified and authorized pursuant to a submission to our approved NDA or NDA supplement which could result in further delay. Further, we will also need to verify, such as through comparability or bridging studies, that any new or modified manufacturing processes will produce our product candidate according to the specifications previously submitted to the FDA, the EMA or comparable foreign regulatory authorities. The delays associated with the verification of a new third- party manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third- party manufacturer may possess technology related to the manufacture of our product candidate that such third- party manufacturer owns independently. This would increase our reliance on such third- party manufacturer or require us to obtain a license from such third- party manufacturer in order to have another third- party manufacturer manufacture our product candidates. We may be unsuccessful in demonstrating the comparability of clinical supplies to those previously allowed into clinical development by the FDA, the EMA or comparable foreign regulatory authorities which could require the conduct of additional studies or clinical trials. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue **. Finally, legislative proposals are pending that, if enacted, could negatively impact U. S. funding for certain biotechnology providers, including some of our vendors, that may have relationships with certain foreign governments or are viewed as posing a threat to national security. This could result in our inability to continue to engage with one or more of our vendors or impair our ability to contract with new vendors, which could result in supply delays or shortages, clinical trial delays and the need to engage new vendors in a competitive marketplace** . Our current and anticipated future dependence upon third parties for the manufacture of any product candidates we develop may adversely affect our development programs and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. We may from time to time be dependent on single- source suppliers for some of the components and materials used in our product candidates. Although we currently do not use any single- source supplier, we may from time to time depend on such suppliers for some of the components and materials used in our product candidates. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single- source suppliers of raw materials, components, key processes and finished goods could expose us to several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single- source supplier or service provider could lead to supply delays or interruptions which

would damage our business, financial condition, results of operations and prospects. If we are required to switch to a replacement supplier, the manufacture and delivery of our product candidates could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. In the event that we should depend on single-source suppliers, we would seek to maintain adequate inventory of the single source components and materials used in our products; however, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our investigational medicines. We may enter into collaborations with third parties for the research, development and commercialization of certain of our product candidates. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates. We may seek third- party collaborators for the research, development and commercialization of certain of our product candidates. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into. Collaborations involving our research programs or our product candidates pose numerous risks to us, including the following: • collaborators would 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 programs, preclinical studies or clinical trials, provide insufficient funding for programs, preclinical studies or clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; • collaborators may be acquired by a third party having competitive products or different priorities, causing the emphasis on our product development or commercialization program under such collaboration to be delayed, diminished or terminated; • collaborators 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 obtain, maintain, enforce or defend our intellectual property or proprietary 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 product candidates or that result in costly litigation or arbitration that diverts management attention and resources; • we may lose certain valuable rights under certain circumstances, including if we undergo a change of control; • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the affected product candidates; and • collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If our collaborations do not result in the successful development and commercialization of product candidates, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this 10- K apply to the activities of our collaborators. These relationships, or those like them, may require us to incur non- recurring and other charges, increase our near- and long- term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time- consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator' s evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. If conflicts arise between us and our potential collaborators, these parties may act in a manner adverse to us and could limit our ability to implement our strategies. If conflicts arise between us and our potential collaborators, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Our collaborators may develop, either alone or with others, products in related fields that are competitive with our product candidates that are the subject of these collaborations with us. Competing products, either developed by the collaborators or to which the collaborators have rights, may result in the withdrawal of support for our product candidates. Some of our future collaborators could also become our competitors. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, fail to devote sufficient resources to the development and commercialization of products, or merge with or be acquired by a third party who may do any of these things. Any of these developments could harm our product development efforts. If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans. Our

product development and research programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us. Collaborations are complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, reduce the scope of any sales or marketing activities, or increase our own expenditures on the development of the product candidate. We are dependent on third- party vendors to provide certain licenses, products and services and our business and operations, including clinical trials, could be disrupted by any problems with our significant third- party vendors. We engage a number of third- party suppliers and service providers to supply critical goods and services, such as contract research services, contract manufacturing services and ~~IT~~ **information technology** services. Disruptions to the business, financial stability or operations of these suppliers and service providers, including due to strikes, labor disputes or other disruptions to the workforce, for instance, if, as a result of ~~the COVID- 19 pandemic or~~ a ~~similar~~ pandemic or health epidemic, employees are not able to come to work, or to their willingness and ability to produce or deliver such products or provide such services in a manner that satisfies the requirements put forth by the authorities, or in a manner that satisfies our own requirements, could affect our ability to develop and market our future product candidates on a timely basis. If these suppliers and service providers were unable or unwilling to continue to provide their products or services in the manner expected, or at all, we could encounter difficulty finding alternative suppliers. Even if we are able to secure appropriate alternative suppliers in a timely manner, costs for such products or services could increase significantly. Any of these events could adversely affect our results of operations and our business. Risks Related to Regulatory Approval and Other Regulatory and Legal Compliance Matters Our lead product candidates are in clinical development, while all of our other product candidates are still in preclinical development. As an organization, we have only completed one clinical trial and initiated one other Phase 1 clinical trial and ~~two~~ **three** Phase 2 clinical trials and may be unable to do so for any of our other product candidates nor carry out or complete further studies for our lead candidate. Although we are currently in clinical development for two product candidates, we have no experience as a company in conducting, completing and managing the full suite of clinical trials necessary to obtain regulatory approvals, including approval by the FDA, the EMA or comparable foreign regulatory authorities, or in obtaining approval of any of our product candidates. We are early in our development efforts for our product candidates, and we have successfully completed a Phase 1 clinical trial and initiated Phase 2 trials for our lead product candidate, PGN- EDO51, **except in the U. S. where the FDA issued a clinical hold on the initiation of our planned CONNECT2 clinical trial,** and initiated ~~a~~ **an additional** Phase 1 **and a Phase 2** clinical trial for our second product candidate, PGN- EDODM1. We will need to successfully complete IND- or CTA- enabling activities, early- stage, later- stage and pivotal clinical trials, in order to obtain FDA, EMA or comparable foreign regulatory approval to market PGN- EDO51, PGN- EDODM1, ~~and, if advanced, PGN- EDO53, PGN- EDO45, PGN- EDO44~~ and any future product candidates. Carrying out clinical trials and the submission of a successful NDA is a complicated process. We completed our first Phase 1 clinical trial for PGN- EDO51 in the third quarter of 2022, and we began dosing ~~patients~~ **participants** in CONNECT1 in Canada in January 2024. We received clearance from the MHRA **in February 2024** to initiate CONNECT2 in the U. K. ~~in February 2024~~ in boys and young men living with DMD. Based on the observed high ~~levels~~ **tissue concentrations** of oligonucleotide ~~delivery~~ and exon skipping in muscle in our Phase 1 **trial of PGN- EDO51 in HVs, as well as the early data from the low dose (5 mg / kg) cohort in our CONNECT1 Phase 2** trial of PGN- EDO51, we believe that these results could signal the potential for the accumulation of exon 51 skipped transcript and **higher production of** dystrophin protein in muscle tissue with repeated doses of PGN- EDO51 in DMD patients **over a longer treatment period** . However, our belief based on **this data may be erroneous and, to date,** the **FDA** ~~Phase~~ -- **has** ~~1~~ **not allowed the initiation of the planned CONNECT2** clinical trial ~~with HVs~~ **in the U. S., placing that trial on clinical hold. Moreover, we have received communication from Health Canada that dosing of participants in the 5 and 10 mg / kg cohorts in our CONNECT1 Phase 2 study** may ~~be erroneous~~ **continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels in the CONNECT1 study. It is unknown whether Health Canada will allow us to further dose escalate or enroll additional participants in this study** . There can be no assurance that our expectations of higher exon skipping and dystrophin production will be reflected in **continued Phase 2** clinical evaluation of PGN- EDO51 in DMD patients **. In addition, based on our observations in preclinical studies that treatment with PGN- EDODM1 led to robust correction of mis- splicing and myotonia, as well as the robust dose- dependent splicing correction observed in the initial data from the 5 and 10 mg / kg cohorts in our FREEDOM Phase 1 study, we believe PGN- EDODM1 has the potential to lead to meaningful functional improvements with repeat dosing over time. However,**

our belief based on this data may be erroneous. There can be no assurance that our expectations of robust splicing correction and improved functional outcomes will be reflected in continued clinical evaluation of PGN- EDODM1 in DM1 patients, including in our ongoing FREEDOM2 MAD study . Although we completed a Phase 1 clinical trial for our lead product candidate **and have several additional clinical trials ongoing** , we have not completed any additional clinical trials, **and** have limited experience as a company in preparing, submitting and prosecuting regulatory filings. In addition, we have had limited interactions with the FDA, the EMA and comparable foreign regulatory authorities and cannot be certain how many clinical trials of PGN- EDO51, PGN- EDODM1, ~~PGN- EDO53, PGN- EDO45, PGN- EDO44~~ or any other product candidates will be required or how such trials should be designed. For example, the FDA has approved at least four drugs based on their minimal dystrophin production, and it is our belief that we may be able to pursue an accelerated approval pathway for PGN- EDO51 on that same basis **, assuming we continue to see increases in exon skipping and dystrophin production with higher doses and a longer treatment period** . The FDA has **previously** provided feedback on our clinical trials for PGN- EDO51, **as well as for PGN- EDODM1,** and we ~~are addressing~~ **have addressed** their feedback in our clinical trial designs ~~to support the~~ **. To date, we have not received FDA feedback on any** potential ~~for~~ accelerated approval **pathway for PGN- EDO51 and currently a clinical hold is in place for the initiation of CONNECT2 in the U. S** . We may be unable to successfully **resolve our current clinical hold** and efficiently execute and complete necessary clinical trials **for our product candidates** in a way that leads to regulatory submission and approval of any of our product candidates **, including potentially any accelerated approval** . We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our current or planned clinical trials, could prevent us from or delay us in submitting NDAs for and commercializing our product candidates. Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time- consuming and uncertain and may prevent us from obtaining approvals for the commercialization of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired. Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the U. S., the EMA and comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have no experience as a company in submitting and supporting the applications necessary to gain marketing approvals and may need to rely on third parties to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate' s safety and effectiveness. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The process of obtaining marketing approvals, both in the U. S. and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Of the large number of products in development, only a small percentage successfully complete the FDA, EMA or foreign regulatory approval processes and are commercialized. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non- approval or restrictions on approval. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA, the EMA and comparable foreign regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate **. Moreover, the U. S. Supreme Court' s July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which FDA' s regulations, policies, and decisions may become subject to increasing legal challenges, delays, and / or changes** . If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired. The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for NDA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage. Clinical trial failure may result from a multitude of factors including flaws in trial design, dose selection, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits, and failure in clinical trials can occur at any stage. Companies in the drug development industry frequently suffer setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from clinical trials is susceptible to varying interpretations, and regulators may not interpret our data as favorably as we

do, which may further delay, limit or prevent marketing approval. The FDA or any foreign regulatory authority could delay, limit or deny approval of a product candidate for many reasons, including because the FDA or such other regulatory authority: • may disagree with the design or implementation of our trials; • may not deem a product candidate to be safe or effective for its intended uses; • determines that the product candidate does not have an acceptable benefit- risk profile; • may not agree that the data collected from preclinical studies and clinical trials are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval, and may impose requirements for additional preclinical studies or clinical trials; • may determine that adverse events experienced by participants in our clinical trials represent an unacceptable level of risk; • may determine that the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval; • may not accept clinical data from trials that are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the U. S.; • may disagree regarding the formulation, labeling and / or specifications; • may not approve the manufacturing processes associated with a product candidate or may determine that a manufacturing facility does not have an acceptable compliance status; • may change approval policies or adopt new regulations; or • may not file a submission due to, among other reasons, the content or formatting of the submission. Even if we eventually complete clinical testing and receive approval of an NDA or foreign marketing application for any product candidates, the FDA, EMA or applicable foreign regulatory authority may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post- market clinical trials. For example, we expect that the FDA will require a ~~post- marketing~~ confirmatory trial of PGN- EDO51, if it is approved under the accelerated approval regulations ~~requiring applicants to demonstrate clinical benefit in post- approval studies~~. The FDA, EMA or the applicable foreign regulatory authority also may approve or authorize for marketing a product candidate for a more limited indication or patient population that we originally request, and the FDA, EMA or applicable foreign regulatory authority may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any of these restrictions or commitments could render an approved product not commercially viable, which would materially adversely impact our business and prospects. Obtaining and maintaining marketing approval or commercialization of our product candidates in the U. S. does not mean that we will be successful in obtaining marketing approval of our product candidates in other jurisdictions. Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue. In order to market and sell our product candidates in the EU and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the U. S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U. S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the U. S. on a timely basis, if at all. Approval by the FDA does not ensure approval by the EMA or regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U. S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. Furthermore, **now that** ~~since the withdrawal of~~ the U. K. ~~from~~ **is no longer part of** the EU, a separate authorization is needed to market medicinal products in ~~Great Britain~~ **the U. K** . We may not be able to file for marketing approvals and may not receive the necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue. Any delay in obtaining, or an inability to obtain, any marketing approvals would prevent us from commercializing any product candidates in the U. K. and / or the EU and / or other foreign jurisdictions and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the U. K. and / or the EU and / or other foreign jurisdictions for our product candidates, which could significantly and materially harm our business. We may attempt to seek approval from the FDA or comparable foreign regulatory authorities, where applicable, under the accelerated approval pathways. We may fail to obtain approval under such accelerated approval pathways. Moreover, these pathways may not lead to a faster development, regulatory review or approval process and do not increase the likelihood that our product candidates will receive marketing approval. We may in the future seek accelerated approval, where applicable, under the FDA' s accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life- threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than ~~irreversible morbidity or mortality, or~~ IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA likely would require that we perform adequate and well- controlled post- marketing clinical trials to confirm the product' s clinical benefit. These confirmatory trials must be completed with due diligence. Under FDORA, the FDA is permitted to require, as appropriate, that a post- approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug' s predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post- approval confirmatory study or submit timely reports to the agency on their progress. **We have reported encouraging early results from the first cohort in our Phase 2 CONNECT1 study of PGN- EDO51 and believe that with a longer treatment period and higher doses of PGN-EDO51, we may see higher levels of exon skipped transcript potentially resulting in significant increases in dystrophin.** If

we **continue to** receive positive results from our ~~Phase 2 trials~~ **CONNECT1 study and receive positive results from the CONNECT2 study** for PGN- EDO51 that show an acceptable safety and tolerability profile; a clinically meaningful increase in dystrophin levels, a surrogate endpoint, in the biceps of DMD patients; and robust exon skipping levels in the same tissue ~~,~~**;** we intend to pursue this accelerated approval pathway subject to discussions with the FDA. However, **we have received communication from Health Canada that dosing of participants in the 5 and 10 mg / kg cohorts may continue at their current dose levels, but currently Health Canada will not allow us to dose escalate** ~~our~~ **or enroll additional participants in our CONNECT1** Phase 2 **trial and the initiation of our CONNECT2 Phase 2 trial is on** clinical **hold in the U. S. Even if we obtain clearance from Health Canada to further dose escalate and enroll more participants in the CONNECT1** trial **and we obtain clearance from the FDA to initiate our CONNECT2 Phase 2 trial in the U. S., these Phase 2 trials** may fail to produce such **supportive clinical** data, and we may be unable to pursue the accelerated approval pathway as planned **. To date we have not received FDA feedback on any potential accelerated approval pathway for PGN- EDO51** . In addition, the FDA currently requires, unless otherwise informed by the agency, pre- approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product' s accelerated approval will eventually be converted to a full approval. In the EU, under the centralized procedure, the EMA' s **CHMP** ~~Committee for Medicinal Products for Human Use~~ may perform an accelerated assessment of a marketing authorization application. Applicants requesting an accelerated assessment procedure must justify that the product candidate is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA or similar foreign regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA or similar application for accelerated approval or any other form of expedited development or review. Similarly, there can be no assurance that after subsequent FDA or similar foreign regulatory authorities feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development or review, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or other expedited development or review for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development or review will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development or review for our product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate, and could harm our competitive position in the marketplace. We may seek one or more designations or expedited programs for one or more of our product candidates, but we might not receive such designations or be allowed to proceed on expedited program pathways, and even if we do and proceed on such expedited program pathways in the future, such designations or expedited programs may not lead to a faster development or regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive marketing approval in the U. S. We have received fast **-** track designation for PGN- EDODM1 for the treatment of DM1 and may seek fast **-** track designation for some of our other product candidates. If a drug is intended for the treatment of a serious or life- threatening condition and nonclinical or clinical data for the drug demonstrates the potential to address an unmet medical need for such a condition, the drug sponsor may apply for fast **-** track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it for any of our other product candidates. Even with fast **-** track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast **-** track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast **-** track designation alone does not guarantee qualification for the FDA' s priority review procedures. We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review **and take action on** an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with

respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six- month review cycle or at all. We may pursue orphan drug designation for certain of our product candidates, and we may not be able to obtain such designation, or obtain or maintain the benefits of such designation including orphan drug exclusivity, and even if we do, that exclusivity may not prevent regulatory authorities from approving other competing products. In September 2023, the FDA granted ~~Orphan~~ **orphan** ~~Drug~~ **drug** ~~Designation~~ **designation** to PGN-EDODM1 for the treatment of DM1 **and in March 2024, the FDA granted orphan drug designation to PGN- EDO51 for the treatment of DMD patients whose mutations are amenable to an exon 51- skipping approach** . We intend to seek orphan drug designation for some of our **other** product candidates; however, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, defined as a patient population of fewer than 200, 000 in the U. S., or a patient population greater than 200, 000 in the U. S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U. S. Orphan drug designation must be requested before submitting an NDA. A similar regulatory scheme governs orphan products in the EU. Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and application fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. In addition, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same product for the same therapeutic indication for seven years. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition. Further, even if we obtain orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted **. A marketing application for a product candidate with RPDD, if approved, may not meet the eligibility criteria for a Priority Review Voucher, or PRV, or the RPDD program may sunset before the FDA is able to consider eligibility for a voucher. Designation of a drug as a product for a rare pediatric disease does not guarantee that a marketing application for such drug will meet the eligibility criteria for a rare pediatric disease PRV at the time the application is approved. While we have received RPDD from the FDA for PGN- EDO51 for the treatment of DMD patients who are amenable to exon 51 skipping, we would need to request a rare pediatric disease PRV in the marketing application of PGN- EDO51. The FDA may determine that any such marketing application, if approved, does not meet the eligibility criteria for a PRV. The FDA' s rare pediatric disease priority review voucher program began to sunset on December 20, 2024 on failure to pass a continuing resolution package that included its reauthorization. Under the amended statutory provisions, after December 20, 2024, the FDA may award rare pediatric disease PRVs for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers. We understand that the FDA continues to review designation requests despite this program beginning to sunset. Congress may vote to reauthorize this program, but its future remains unknown at this time. If a marketing application for PGN- EDO51 is not approved prior to September 30, 2026 for any reason, regardless of whether it meets the criteria for a rare pediatric disease PRV, it will not be eligible for a PRV, unless the authority for FDA to award rare pediatric disease PRVs is further extended through federal lawmaking** . We may seek designation for our EDO platform as a designated platform technology, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process. We may seek designation for our EDO platform as a designated platform technology. Under FDORA, a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA for a drug that uses or incorporates the platform technology. Even if we believe our EDO platform meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not

ensure that a drug will be developed more quickly or receive FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation. Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to post- market study requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements. The FDA, the EMA or a comparable foreign regulatory authority may not approve any of our product candidates derived from our platform. However, if the FDA, EMA or comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, conformance with applicable product tracking and tracing requirements, establishment registration and listing, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post- approval. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing studies, and surveillance to monitor the safety and efficacy of the product. Additionally, under FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product' s ability to be marketed. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: • restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls; • restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials; • restrictions on product distribution or use, or requirements to conduct post- marketing studies or clinical trials; • fines, warning letters or other regulatory enforcement action; • refusal by the FDA, the EMA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us; • product seizure or detention, or refusal to permit the import or export of products; and • injunctions or the imposition of civil or criminal penalties. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity. In addition, the FDA' s, EMA' s and other foreign regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability. Any product candidate for which we obtain marketing approval will be subject to restrictions, such as the laws and regulations prohibiting the promotion of off- label uses, or may need to be withdrawn from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved. The FDA, EMA and other foreign regulatory authorities closely regulate the post- approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA, EMA and other foreign regulatory authorities impose stringent restrictions on manufacturers' communications regarding off- label use. In particular, a product may not be promoted for uses that are not approved by the FDA, EMA and other foreign regulatory authorities as reflected in the product' s approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off- label uses, we may be subject to enforcement action for off- label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off- label use and has enjoined several companies from engaging in off- label promotion. The government has also required companies to enter into consent decrees and / or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition. In addition, later discovery of previously unknown problems with our medicines, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including: • restrictions on such medicines, manufacturers or manufacturing processes; • restrictions on the labeling or marketing of a medicine; • restrictions on the distribution or use of a medicine; • requirements to conduct post- marketing clinical trials; • receipt of warning or untitled letters; • withdrawal of the medicines from the market; • refusal to approve pending applications or supplements to approved applications that we submit; • recall of medicines; • fines, restitution or disgorgement of profits or revenue; • suspension or withdrawal of marketing approvals; • suspension of any ongoing clinical trials; • refusal to permit the import or export of our medicines; • product seizure; and Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any product candidates we develop and adversely affect our business, financial condition, results of operations and prospects. Additionally, if any of our product candidates receive marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits outweigh

its risks, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients and a communication plan to healthcare practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including: • regulatory authorities may suspend or withdraw approvals of such product candidate; • regulatory authorities may require additional warnings on the label; • we may be required to change the way a product candidate is administered or conduct additional clinical trials; • we could be sued and held liable for harm caused to patients; and We and our contract manufacturers are subject to significant regulation. The manufacturing facilities on which we rely may not continue to meet regulatory requirements, which could materially harm our business. All entities involved in the preparation of product candidates for clinical trials or commercial sale, including any contract manufacturers, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late- stage clinical trials must be manufactured in accordance with cGMP regulations. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract ~~manufacturer~~ **manufacturers** must supply all necessary documentation in support of an NDA on a timely basis and must adhere to the FDA' s cGMP regulations enforced through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third- party contractors must pass a pre- approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre- approval plant inspection, FDA approval of the products will not be granted. The regulatory authorities also may, at any time following approval of a product for sale, audit any of our future manufacturing facilities or those of our third- party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and / or time- consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business. If we or any of our third- party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product, or revocation of a pre- existing approval. Any such consequence would severely harm our business, financial condition and results of operations. If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur significant costs. We and any contract manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health, and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at third- party facilities. We also could incur significant costs associated with civil or criminal fines and penalties. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations and permitting requirements. These current or future laws, regulations and permitting requirements may impair our research, development or production efforts. Failure to comply with these laws, regulations and permitting requirements also may result in substantial fines, penalties or other sanctions or business disruption. Any third- party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could in turn have a material adverse effect on our business, financial condition, results of operations and prospects. Shutdowns or disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business. **Currently, federal agencies in the U. S. are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U. S. market could be impacted.** 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, statutory, regulatory and policy changes, the FDA' s ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies 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 slow 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, including for 35 days beginning on December 22, 2018, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. During the COVID- 19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA' s inability to complete required inspections for their applications. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Our relationships with healthcare providers, physicians and third- party payors will be subject to applicable anti- kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. Healthcare providers, physicians and third- party payors play a primary role in the recommendation and prescription of any product candidates that we develop for which we obtain marketing approval. Our future arrangements with third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, without limitation, the federal Anti- Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations. For more information, see " Business – Healthcare Regulation – Other Healthcare Laws " in this 10- K. Additionally, we are subject to state and foreign equivalents of each of these healthcare laws and regulations, among others, some of which may be broader in scope and may apply regardless of the payor. Many U. S. states have adopted laws similar to the federal Anti- Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and / or the Pharmaceutical Research and Manufacturers of America' s Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU **and U. K** . The provision of benefits or advantages to induce or reward improper performance generally is typically governed by the national anti- bribery laws of European Union Member States, and the Bribery Act 2010 in the U. K. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001 / 83 / EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the U. K. despite its departure from the EU. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician' s employer, his or her competent professional organization and / or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. The scope and enforcement of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. We have entered into consulting and scientific advisory board arrangements with physicians and other healthcare providers, including some who could influence the use of our product candidates, if approved. Compensation under some of these arrangements includes the provision of stock or stock options in addition to cash consideration. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and

individual imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected. Healthcare legislative reform discourse and potential or enacted measures may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain. Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the U. S. and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. For more information, see " Business – Healthcare Regulation – Healthcare Reform and Legislative Updates " in this 10- K. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will 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 our product candidates or additional pricing pressures. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and / or impose price controls may adversely affect: • the demand for our product candidates, if we obtain regulatory approval; • our ability to set a price that we believe is fair for our products, if licensed; • our ability to generate revenue and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital. We expect that other healthcare reform measures may be adopted in the future, which may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for our products. Any denial in coverage or reduction in reimbursement from Medicare or other government- funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our products. It is not clear how other future potential changes to the ACA will change the reimbursement model and market outlook for our current and future product candidates. Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk of fraud or other misconduct by our employees, consultants and partners, and in our clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the U. S. and abroad, 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, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the European Commission and other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee 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 government investigations or other actions or lawsuits stemming from a failure to comply with these 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, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions. Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the U. S. and require us to develop and implement costly compliance programs. We are subject to numerous laws and regulations in each jurisdiction outside the ~~United States~~ **U. S.** in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. The Foreign Corrupt Practices Act ~~(~~**, or** FCPA ~~)~~**,** prohibits any U. S. individual or business from paying, offering, or authorizing the provision of money or anything of value, directly or indirectly through parties, to any foreign official, official of a public international organization, or political party official or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U. S. to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti- bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA. Compliance with the FCPA and other anti-corruption laws potentially applicable to our business is expensive and difficult, particularly in countries in which corruption is a

recognized problem. In addition, compliance with the FCPA and other anti- corruption laws presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Various U. S. export and sanctions laws, regulations and executive orders also restrict the use and dissemination outside of the U. S., or the sharing with certain non- U. S. nationals, of certain products and technical data relating to those products. Furthermore, such export and sanctions laws include restrictions or prohibitions on the sale or supply of certain products and services to U. S. embargoed countries or sanctioned countries, governments, persons and entities. Our expansion outside of the U. S. has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain drugs and drug candidates outside of the U. S., which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA and export and sanctions laws can result in significant civil and criminal penalties, imprisonment, the loss of export or import privileges, debarment, breach of contract and fraud litigation, reputational harm, and other consequences. Indictment alone under the FCPA can lead to suspension of the right to do business with the U. S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long- term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U. S. exchanges for violations of the FCPA' s accounting provisions. We are subject to stringent data protection, privacy, and security laws, regulations, standards and contractual obligations and actual or perceived failure to comply with such requirements could have a material adverse effect on our business, financial condition, results of operations or prospects. We are subject to data privacy and protection laws, regulations, policies, standards and contractual obligations that impose certain requirements relating to the collection, transmission, storage and use of personal information. The legislative and regulatory landscape for data privacy and protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues. Actual or perceived failure to comply with laws and regulations governing personal information could result in government investigations and enforcement actions against us, fines, claims for damages by affected third parties, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects. The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of personal information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer or other processing of personal data, including personal health data, of individuals in the European Economic Area, or EEA, is subject to the EU General Data Protection Regulation, or EU GDPR, as well as national data protection laws in effect in the member states of the EEA, and similar processing of personal data regarding individuals in the U. K. is governed by the U. K. General Data Protection Regulation, or U. K. GDPR and the U. K. Data Protection Act 2018. In this document, " GDPR " refers to both the EU GDPR and the U. K. GDPR, unless specified otherwise ~~. The U. K. GDPR is currently largely in line with the EU GDPR, but the data protection regimes may diverge more in the future~~ . The GDPR imposes stringent requirements on companies that process personal data, including requirements relating to **having a legal basis for** processing ~~health- related and~~ **personal data, stricter requirements relating to** ~~other~~ -- **the processing of** sensitive data **(such as health data)** , **where required by GDPR-** obtaining consent of the individuals to whom the personal data relates, establishing a legal basis for processing, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data that requires the adoption of administrative, physical and technical safeguards to protect such information, providing notification of data breaches to appropriate data protection authorities or data subjects, **requiring data protection impact assessments for high risk processing and** establishing means for data subjects to exercise rights in relation to their personal data and taking certain measures when engaging third- party processors. The GDPR' s definition of personal data includes coded data ~~and it imposes rules relating to informed consent practices and for clinical trials and notices for clinical trial subjects and investigators~~ . Failure to comply with the requirements of the GDPR may result in warning letters, mandatory audits, orders to cease / change the use of data, and financial penalties, including fines, which can be up to 4 % of global revenues or € 20 million (£ 17. 5 million for the U. K.), whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Among other requirements, the GDPR includes restrictions on cross- border transfers of personal data subject to the GDPR to countries outside the EEA / U. K. that have not been found to provide adequate protection to such personal data (third countries), unless a valid GDPR transfer mechanism (for example, the European Commission approved Standard Contractual Clauses, or SCCs, certification to the EU- U. S. Data Privacy Framework (which allows for transfers to relevant U. S.- based organizations who self- certify compliance and participate in the framework) and the U. K. International Data Transfer Agreement / Addendum, or U. K. IDTA) has been put in place. Where relying on the SCCs / U. K. IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. The international transfer obligations under the EEA / U. K. data protection regimes will require significant effort and cost ~~,~~ and may result in us needing to make strategic considerations around where EEA / U. K. personal data is transferred and which service providers we can utilize for the processing of EEA / U. K. personal data. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the

geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. Switzerland has also adopted similar restrictions on transfer of personal data outside of its borders. Although the U. K. is regarded as a third country under the EU' s GDPR, the European Commission has adopted an (adequacy decision) in favor of the U. K., a decision recognizing the U. K. as providing adequate protection under the EU GDPR and enabling data transfers from EU Member States to the U. K. without additional safeguards. However, the U. K. adequacy decision will automatically expire in June 2025 unless the European Commission re- assesses and renews or extends that decision and remains under review by the Commission during this period. The U. K. government has confirmed that personal data transfers from the U. K. to the EEA remain free flowing. ~~The~~ **On October 24, 2024, the** U. K. Government ~~has also now~~ introduced ~~a~~ **its** Data ~~Protection~~ **Use** and **Access** ~~Digital Information~~ Bill ~~(~~**, or** U. K. Bill ~~),~~ into the U. K. legislative process ~~. The aim of the U. K. Bill is to reform the U. K.' s data protection regime following Brexit~~ . If passed, the final version of the U. K. Bill may have the effect of further altering the similarities between the U. K. and EEA data protection regime and threaten the U. K. Adequacy Decision from the European Commission. This may lead to additional compliance costs and could increase our overall risk. It is unclear how U. K. data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the U. K. will be regulated in the long term. Although the EU GDPR and the U. K. GDPR currently impose substantially similar obligations it is possible that over time the respective provisions, interpretations and enforcement of the EU GDPR and U. K. GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. The lack of clarity on future U. K. laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of U. K. and EEA personal data and our privacy and data security compliance programs, and could require us to implement different compliance measures for the U. K. and the EEA. If we are unable to implement a valid solution for personal data transfers from the EEA, U. K. or Switzerland to the U. S. or other countries, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data in those jurisdictions. Inability to import personal data from the EEA, U. K. or Switzerland may also restrict our clinical trials activities in those jurisdictions; limit our ability to collaborate with contract research organizations as well as other service providers, contractors and other companies subject to data protection laws in those jurisdictions; and require us to increase our data processing capabilities in those jurisdictions at significant expense. Additionally, other countries outside of the EEA, U. K., and Switzerland have enacted or are considering enacting similar cross- border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business. Given the breadth and depth of applicable data protection obligations, preparing for and complying with the GDPR and similar laws' requirements are rigorous and time intensive and require significant resources and a review of our technologies, systems and practices, as well as those of any third- party collaborators, service providers, contractors or consultants that process or transfer personal data. The GDPR, and other laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Similar privacy and data security requirements are either in place or underway in the U. S. There are numerous data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered or have been implemented at both the state and federal levels. For example, the California Consumer Privacy Act of 2018, or the CCPA, which became effective on January 1, 2020, requires companies that process information of California consumers (as defined under the CCPA) to provide disclosures to such consumers about their data collection, use and sharing practices, provides Californian consumers with new individual data privacy rights, imposes new operational requirements for covered businesses, provides a private right of action for data breaches and creates a statutory damages framework. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws could impact our business activities depending on how such laws are interpreted. Additionally **as of** ~~, effective starting on~~ January 1, 2023, the California Privacy Rights Act, or CPRA ~~will~~ **has** significantly ~~modify~~ **modified** the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also ~~creates~~ **created** a new state agency that will be vested with authority to implement and enforce the CCPA ~~and the CPRA~~ . Many other states **have enacted or** are considering similar legislation, and a broad range of legislative measures also have been introduced at the federal level **. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and / or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. There are also states that are specifically regulating health information. For example, Washington state recently passed a health privacy law that, as of June 30, 2024, regulates the collection and sharing of health information. This law also has a private right of action, which further increases the relevant compliance risk collecting the health information of Washington residents. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and / or passed legislation that regulates the privacy and / or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business**

partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there is discussion in the U. S. Congress of a new comprehensive federal data privacy law to which we may likely become subject, if enacted . Further, regulations promulgated pursuant to HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and referred herein collectively as HIPAA, imposes privacy, security and breach notification obligations on health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, as well as their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities, and their covered subcontractors. HIPAA establishes privacy and security standards that limit the use and disclosure of protected health information, or PHI, and requires the implementation of administrative, physical and technological safeguards to protect the privacy of PHI and ensure the confidentiality, integrity and availability of electronic PHI. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to HIPAA. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements. However, any person may be prosecuted under HIPAA' s criminal provisions either directly or under aiding- and- abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA- covered healthcare provider or research institution that has not satisfied HIPAA' s requirements for disclosure of individually identifiable health information. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. Further, any failure by our third- party collaborators, service providers, contractors or consultants to comply with applicable law, regulations or contractual obligations related to data privacy or security could result in proceedings against us by governmental entities or others. We may also publish privacy policies and other documentation regarding our collection, processing, use and disclosure of personal information and / or other confidential information. Although we endeavor to comply with our published policies and other documentation, we may at times fail to do so or may be perceived to have failed to do so. Despite our efforts, we may not be successful in achieving compliance if our employees or vendors fail to comply with our published policies and documentation. Such failures can subject us to potential international, local, state and federal action if they are found to be deceptive, unfair, or misrepresentative of our actual practices. **All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management' s time and / or divert resources from other initiatives and projects.** Claims that we have violated individuals' privacy rights or failed to comply with data protection laws or applicable privacy notices, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business. ~~We also face a threat of~~ **Any failure or perceived failure by us to comply with any applicable federal, state or foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including** consumer class actions related to these laws and the overall protection of personal information. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business, financial condition, results of operations or prospects **. Further, the use of new and evolving technologies, such as artificial intelligence, in our business may result in spending material resources and presents risks and challenges that can impact our business including by posing security and other risks to our confidential and / or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability** . If any of our product candidates obtains regulatory approval and does not receive appropriate periods of non- patent exclusivity, competitors could enter the market with generic versions of such products more quickly than we expect, which may result in a material decline in sales of our products. Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch- Waxman Amendments to the FDCA, a company may file an abbreviated new drug application, or ANDA, seeking approval of a generic version of an approved innovator product. Under the Hatch- Waxman Amendments, a company may also submit an NDA under section 505 (b) (2) of the FDCA that references the FDA' s prior approval of the innovator product. A 505 (b) (2) NDA product may be for a new or improved version of the original innovator product. The Hatch- Waxman Amendments also provide for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and review) of an ANDA or 505 (b) (2) NDA. In the U. S., once an NDA is approved, the product covered thereby becomes a " reference listed drug " in the FDA' s publication, " Approved Drug Products with Therapeutic Equivalence Evaluations, " or the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of ~~abbreviated new drug applications, or~~ ANDAs ~~,~~ in the U. S. In support of an ANDA, a generic manufacturer generally must show that its product has the same active ingredient (s), dosage form, strength, route of administration, and adequate labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning, in part, that it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Moreover, many states allow or require substitution of therapeutically equivalent generic drugs at the pharmacy level even if the branded drug is prescribed. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug may be lost to the generic product. The FDA may not finally approve an ANDA for a generic product until any applicable period of non- patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non- patent exclusivity for a new drug containing a ~~new chemical entity, or~~ NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously

been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a patent certification that a patent covering the listed drug is invalid unenforceable or will not be infringed by the generic product. In that case, the applicant may submit its application four years following approval of the listed drug and seek to launch its generic product even if we still have patent protection for our product unless an infringement suit is timely filed by the NDA or patent holder in which case the FDA cannot approve the ANDA for 30 months unless a court decision in favor of the generic manufacturer is issued earlier. Three- year exclusivity is given to a drug if it contains an active moiety that has previously been approved, and the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the NDA. This form of marketing exclusivity is known as New Clinical Investigation, or NCI, exclusivity. If our product candidates are approved with only NCI exclusivity, generic manufacturers may file their ANDAs any time following approval of our product candidates and seek to launch their generic products following the expiration of the three year market exclusivity period, even if we still have patent protection for our product unless an infringement suit is timely filed triggering a 30 month stay on approval of the generic product (subject to the disposition of the patent litigation). While we believe that our product candidates may be **NCEs** ~~new chemical entities~~ in the U. S., the FDA may determine, however, that they are not eligible for NCE exclusivity but receive three years of NCI exclusivity instead, if and when FDA approves an NDA for the product. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to any patents exclusivity we may have. If an ANDA applicant certifies to the invalidity or non- infringement of listed patents and an infringement suit is timely filed by the NDA or patent holder, the FDA cannot finally approve the ANDA for 30 months unless a court decision in favor of the generic manufacturer is issued earlier. Accordingly, if any of our product candidates is approved, competitors could file ANDAs for generic versions of these products or 505 (b) (2) NDAs that reference our product candidates. If there are patents listed for our product candidates in the Orange Book, any ANDA and 505 (b) (2) NDA applicants would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. FDORA also requires that the FDA consider therapeutic equivalence determinations for certain Section 505 (b) (2) drugs that are pharmaceutical equivalents to listed drugs relied upon in an application either at the time of approval or up to 180 days post- approval, upon request of the sponsor. These therapeutic equivalence determinations could have an adverse effect on our business. Because we remain early in the research and preclinical development of our product candidates, we cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit. We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license, despite expending a significant amount of resources that could have been focused on other areas of our business. Moreover, if any of our owned or in- licensed patents that are listed in the Orange Book are successfully challenged by way of a patent certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. Risks Related to Commercialization We face substantial competition, which may result in others discovering, developing or commercializing products before us or more successfully than we do. The development and commercialization of new drug products is highly competitive. We face competition with respect to our product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disorders for which we are conducting research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product candidates or that would render our product candidates obsolete or non- competitive. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors. We expect to face competition from existing products and product candidates in development for each of our programs. Currently, patients with DMD are treated with corticosteroids to manage the inflammatory component of the disease. EMFLAZA is an FDA- approved corticosteroid marketed by PTC. Individuals with DMD also use prednisone or prednisolone off- label. In addition, there are several FDA- approved exon skipping drugs: EXONDYS 51 and VYONDYS 53, which are naked PMOs approved for the treatment of DMD patients amenable to exon 51 and exon 53 skipping, respectively, and are marketed by Sarepta; and VILTEPSO, a naked PMO approved for the treatment of DMD patients amenable to exon 53 skipping, which is marketed in the U. S. by NS Pharma, Inc. **Notably, it was reported in May 2024 that the Phase 3, confirmatory study of VILTEPSO failed to meet the primary endpoint, Time to Stand from Supine, measured as velocity rise per second.** Companies focused on developing treatments for DMD that target dystrophin **production** , as our DMD program does, include ~~Sarepta with SRP- 5051, a peptide- linked PMO currently being evaluated in a Phase 2b clinical trial for patients amenable to exon 51 skipping;~~ Dyne **,** with DYNE- 251, an antibody- conjugated PMO that targets exon 51 skipping in a Phase 1 / 2 clinical trial; BioMarin **,** with BMN- 351, a phosphorothioate oligonucleotide that targets exon 51 skipping currently in preclinical development; and Wave **,** with WVE- N531, a stereopure oligonucleotide in a

Phase 1 / 2 clinical trial for patients amenable to exon 53 skipping. In **November 2024, Sarepta announced it was discontinuing development of SRP- 5051, a peptide- linked PMO for patients amenable to exon 51 skipping due to certain adverse events experienced by patients. In** addition, several companies are developing gene therapies to treat DMD. These include ELEVIDYS **,** ~~(SRP- 9001)~~ which was approved in June 2023 for treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation in the DMD gene. In **June 2024, the FDA granted approval of** an **expansion to the labeled indication for ELEVIDYS to include individuals** ~~interim readout of a recent Phase 3 trial (EMBARK), which is still ongoing, patients~~ with DMD ~~between ages~~ **with a confirmed mutation in the DMD gene who are at least** 4 ~~through 7~~ years **of age, granting traditional approval for** ~~treated with ELEVIDYS did not show statistically significant benefit on the North Star Ambulatory~~ **ambulatory patients and accelerated approval for** ~~Assessment, which was the primary endpoint. ELEVIDYS showed statistically significant results on~~ **non** ~~all key pre-~~ **ambulatory patients. Continued approval for non** ~~specified secondary endpoints, time to rise and 10-~~ **ambulatory** ~~meter walk / run test. Based on the interim read- out from EMBARK, Sarepta has filed an efficacy supplement to its BLA to expand the label of ELEVIDYS to encompass " treatment of~~ DMD patients **may be contingent upon verification** ~~with a confirmed mutation in the DMD gene. " The FDA accepted the filing~~ of **clinical benefit in** ~~the efficacy supplement and has given the application priority review with~~ a **confirmatory trial** ~~review goal date of June 21, 2024~~. In addition, several other companies are developing investigational gene therapies to treat DMD, including ~~Pfizer Inc.' s PF- 06939926, fordadistrogene movaparvovec, which is currently being assessed in a Phase 3 clinical trial, Sarepta' s Galgt2 gene therapy program, and~~ Solid Biosciences Inc.' s SGT- 003 and REGENXBIO Inc.' s RGX- 202, currently in **Phase 1 and Phase 2** clinical development **, respectively** . Gene editing treatments that are in preclinical development are also being pursued by Vertex and Sarepta. We are also aware of several companies targeting non- dystrophin mechanisms for the treatment of DMD, including Edgewise with EDG- 5506, a muscle stabilizer that is currently in clinical development and ~~givinostat~~ **Italfarmaco S. p. A.** , ~~a~~ **with Duvyzat, an oral histone deacetylase, or** HDAC inhibitor, that reduces fibrosis in patients with DMD and **was approved by the FDA in March of 2024 for the treatment of DMD in patients six years of age and older, and** is ~~currently~~ under review by the ~~FDA and~~ EMA. For DM1, there are currently no approved therapies to treat the underlying cause of the disease. Pipeline candidates currently in development to treat DM1 include several approaches that target DMPK RNA. These include AOC 1001, an antibody linked siRNA in Phase **3** ~~1 / 2~~ clinical development ~~with a global Phase 3 study planned for initiation in the second quarter of 2024~~ by Avidity; DYNE- 101, an antibody conjugated antisense oligonucleotide in **Phase 1 / 2** clinical development by Dyne; ~~and~~ VX- 670, a peptide conjugated PMO in Phase ~~1 2~~ by Entrada and Vertex **; and ARO- DM1, a conjugated siRNA in Phase 1 / 2 clinical development by Arrowhead and Sarepta** . There are additional approaches under development such as ATX- 01, a microRNA that modulates expression of MBNL1 by Arthex Biotech S. L., that ~~recently received IND clearance~~ **is in Phase 1 clinical development** . Another small molecule, tideglusib, which is a GSK3- ß inhibitor is in clinical development by AMO ~~Pharma Ltd.~~ for the congenital phenotype of DM1 ~~, recently failed to meet primary endpoint in a pivotal study~~ . Several gene editing **and gene delivery** treatments are in **discovery or** preclinical development by Vertex ~~; an~~ **and Kate Therapeutics Inc. (recently acquired** ~~artificial site- specific RNA endonuclease gene therapy is being developed~~ by ~~Enzerna~~ **Novartis)** ; Design ~~Therapeutics, Inc.~~ is developing an approach to prevent formation of CUG hairpins; Expansion **and Arrakis are** ~~Therapeutics, Inc. is~~ developing an approach utilizing the interaction of small molecules with RNA in preclinical development; and therapeutics based on biomolecular condensate biology in preclinical development by Dewpoint and Pfizer. We will also compete more generally with other companies developing alternative scientific and technological approaches, including other companies working to develop conjugates with oligonucleotides for extra- hepatic delivery, including Alnylam, Aro, Arrowhead, Avidity, Dicerna **Pharmaceuticals, Inc. (acquired by Novo Nordisk)** , Dyne, Entrada, Ionis, NeuBase, PYC and Sarepta, as well as gene therapy and gene editing approaches. Many of the companies against which we compete or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Accordingly, our competitors may be more successful than us in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non- competitive. Additionally, mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, 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, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any of our products, if approved. Competitive products or technological approaches may make any products we develop, or our EDO platform, obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products, if approved, could be adversely affected. Even if one or more of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third- party payors and others in the medical community necessary for commercial success. If any of our product candidates progresses successfully through clinical development and receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians,

patients, third- party payors and others in the medical community. Sales of medical products depend in part on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost- effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost- effective as compared with competing treatments. Efforts to educate the medical community and third- party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including: • the efficacy and safety of such product candidates as demonstrated in clinical trials; • the potential advantages and limitations compared to alternative treatments; • the effectiveness of sales and marketing efforts; • the cost of treatment in relation to alternative treatments; • the clinical indications for which the product is approved; • the convenience and ease of administration compared to alternative treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the strength of marketing and distribution support; • the timing of market introduction of competitive products; • the availability of third- party coverage and adequate reimbursement; • the prevalence and severity of any side effects; and • any restrictions on the use of our products, if approved, together with other medications. If the market opportunities for any product candidates we develop are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our programs are small, and the addressable patient population even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth. We focus our research and product development on treatments for rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. Our target patient populations are relatively small, and as a result, the pricing and reimbursement of our product candidates, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell product candidates will be adversely affected. The estimates of market opportunity and forecasts of market growth included in this 10- K **, if any,** may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all. Market opportunity estimates and growth forecasts included in this 10- K **, if any,** are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. The estimates and forecasts included in this 10- K relating to size and expected growth of our target market **, if any,** may prove to be inaccurate. Even if the markets in which we compete meet ~~the~~ **any** size estimates and **/ or** growth forecasts included in this 10- K, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties. The pricing and third- party payor coverage and reimbursement status of newly approved products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our future product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue. In the U. S. and markets in other countries, patients generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. For more information, see " Business – Healthcare Regulation – Coverage and Reimbursement " in this 10- K. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U. S., the decisions about coverage and reimbursement for new products under the Medicare program are made by the Centers for Medicare & Medicaid Services, or CMS. Private payors tend to follow CMS to a substantial degree. However, one payor' s determination to provide coverage for a product does not assure that other payors will also provide coverage for the drug product. Further, a payor' s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement agencies in the EU may be more conservative than CMS. Factors payors consider in

determining reimbursement are based on whether the product is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; • cost- effective; and • neither experimental nor investigational. Additionally, 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 U. S. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Outside the U. S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in the EU, the U. K., Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product, possibly for lengthy periods of time. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the U. S. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for product candidates. Accordingly, in markets outside the U. S., the reimbursement for our product candidates may be reduced compared with the U. S. and may be insufficient to generate commercially reasonable revenues and profits. If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates if any are approved. We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties. In the future, we may build a sales and marketing infrastructure to market certain of our product candidates if they receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time- consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Factors that may inhibit our efforts to commercialize our products on our own include: • our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel; • the inability of sales personnel to educate adequate numbers of physicians on the benefits of any future products; • the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors; • the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability; • restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and • unforeseen costs and expenses associated with creating an independent sales and marketing organization. If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. Risks Related to Our Intellectual Property If we or our licensors are unable to obtain, maintain and defend patent and other intellectual property protection for any product candidates or technology, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully develop and commercialize our product candidates or our technology may be adversely affected due to such competition. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the U. S. and other jurisdictions. We and our licensors have sought, and will seek, to protect our proprietary position by filing additional patent applications in the U. S. and abroad related to certain technologies and our platform that are important to our business. However, our patent portfolio is at ~~an~~ **a somewhat** early stage; ~~except for~~ **there are two issued patents (** one ~~issued~~ **of which is a European** patent **validated in five countries)** ~~and seven applications currently under examination~~ , which we in- licensed from Oxford University **Innovation Limited, or OUI,** and the Medical Research Council of United Kingdom Research and Innovation, **or MRC, and** substantive examination **of more than half** of the currently pending patent applications we own or license has yet to begin. In addition, there can be no assurance as to whether or

when our patent applications will issue as granted patents. Our ability to stop third parties from making, using, selling, marketing, offering to sell, importing and commercializing our product candidates and our technology is dependent upon the extent to which we have rights under valid and enforceable patents and other intellectual property that cover our platform and technology. If we are unable to secure, maintain, defend and enforce patents and other intellectual property with respect to our product candidates and our technology, it would have a material adverse effect on our business, financial condition, results of operations and prospects. Our pending PCT patent applications are not eligible to become issued patents until, among other things, we file a national stage patent application within 30 to 32 months, depending on the jurisdiction, from such application' s priority date in the jurisdictions in which we are seeking patent protection. Similarly, our pending provisional patent applications are not eligible to become issued patents until, among other things, we file a non- provisional patent application within 12 months of such provisional patent application' s filing date. If we do not timely file such national stage patent applications or non- provisional patent applications, we may lose our priority date with respect to such PCT or provisional patent applications, respectively, and any patent protection on the inventions disclosed in such PCT or provisional patent applications, respectively. While we and our licensors intend to timely file national stage and non- provisional patent applications relating to our PCT and provisional patent applications, respectively, we cannot predict whether any such patent applications will result in the issuance of patents. If we or our licensors do not successfully obtain issued patents, or, if the scope of any patent protection we or our licensors obtain is not sufficiently broad, we will be unable to prevent others from using our product candidates or our technology or from developing or commercializing technology and products similar or identical to ours or other competing products and technologies. Any failure to obtain or maintain patent protection with respect to our product candidates or our EDO platform would have a material adverse effect on our business, financial condition, results of operations and prospects. The patent prosecution process is expensive, time- consuming and complex, and we and our licensors may not be able to file, prosecute, maintain, defend, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. We and our licensors may not be able to obtain, maintain or defend patents and patent applications due to the subject matter claimed in such patents and patent applications being in the public domain. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non- disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we would not be able to prevent any third party from using any of our technology that is in the public domain to compete with our product candidates. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of patent rights are highly uncertain. Our pending and future owned and licensed patent applications may not result in patents being issued which protect our technology or product candidates, effectively prevent others from commercializing competitive technologies and product or otherwise provide any competitive advantage. In fact, patent applications may not issue as patents at all, and even if such patent applications do issue as patents, they may not issue in a form, or with a scope of claims, that will provide us with any meaningful protection, prevent others from competing with us or otherwise provide us with any competitive advantage. In addition, the scope of claims of an issued patent can be reinterpreted after issuance, and changes in either the patent laws or interpretation of the patent laws in the U. S. and other jurisdictions may diminish the value of our patent rights or narrow the scope of our patent protection. Furthermore, our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non- infringing manner. Third parties have developed technologies that may be related or competitive to our own technologies and product candidates and may have filed or may file patent applications, or may have obtained issued patents, claiming inventions that may overlap or conflict with those claimed in our owned or licensed patent applications or issued patents. We may not be aware of all third- party intellectual property rights potentially relating to our current and future product candidates and technology. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know for certain whether the inventors of our owned or licensed patents and patent applications were the first to make the inventions claimed in any owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or ruled unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U. S. and other jurisdictions. For example, we may be subject to a third- party submission of prior art to the USPTO, challenging the validity of one or more claims of our owned or licensed patents. Such submissions may also be made prior to a patent' s issuance, precluding the granting of a patent based on one of our owned or licensed pending patent applications. We may become involved in opposition, derivation, re- examination, inter partes review, post- grant review or interference proceedings and similar proceedings in foreign jurisdictions (for example, opposition proceedings) challenging our owned or licensed patent rights. In addition, a third party may claim that our owned or licensed patent rights are invalid or unenforceable in a litigation. An adverse result in any litigation or patent office proceeding could put one or more of our owned or licensed patents at risk of being invalidated, ruled unenforceable or interpreted narrowly and could allow third parties to commercialize products identical or similar to our product candidates and compete directly with us, without payment to us. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post- grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of

patentability. Such challenges and proceedings may result in loss of patent rights, exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and our product candidates. Such challenges and proceedings may also result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Moreover, there could be public announcements of the results of hearings, motions or other interim proceedings or developments related to such challenges and proceedings. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Furthermore, patents have a limited lifespan. In the U. S., the expiration of a patent is generally 20 years from the earliest date of filing of the first non- provisional patent application to which the patent claims priority. Patent term adjustments and extensions may be available; however, the overall term of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent and other intellectual property rights may not provide us with sufficient rights to exclude others from commercializing products similar or identical to our technology and our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects. Our rights to develop and commercialize any product candidates are subject and may in the future be subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business. We are and expect to continue to be reliant upon third- party licensors for certain patent and other intellectual property rights that are important or necessary to the development of our technology and product candidates. For example, we rely on a license from ~~Oxford University Innovation Limited (~~OUI ~~),~~ and ~~the Medical Research Council of United Kingdom Research and Innovation, or~~ MRC, to certain patent rights and know- how of OUI and MRC ~~, or the OUI / MRC License~~ . The OUI / MRC License imposes, and we expect that any future license agreement will impose, specified diligence, milestone payment, fee payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. Furthermore, our licensors have, or may in the future have, the right to terminate a license if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. If our license agreements are terminated, we may lose our rights to develop and commercialize product candidates and technology, lose patent protection, experience significant delays in the development and commercialization of our product candidates and technology, and incur liability for damages. If these in- licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, our competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our product candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with our product candidates and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects. Disputes may arise regarding intellectual property subject to a licensing agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties; • the extent to which our technology, product candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement; • the sublicensing of patent and other intellectual property rights under our license agreements; • our diligence, development, regulatory, commercialization, financial or other obligations under the license agreement and what activities satisfy those diligence obligations; • the inventorship and ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and • the priority of invention of patented technology. In addition, the OUI / MRC License is, and future license agreements are likely to be, complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over intellectual property that we have licensed or any other dispute related to our license agreements prevent or impair our ability to maintain our license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. While the OUI / MRC License grants certain exclusive patent and technology rights to us, license agreements we may enter into in the future may be non- exclusive. Accordingly, third parties may also obtain non- exclusive licenses from such licensors with respect to the intellectual property licensed to us under such license agreements. Accordingly, these license agreements may not provide us with exclusive rights to use such licensed patent and other intellectual property rights, or may not provide us with exclusive rights to use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and our product candidates. Moreover, some of our in- licensed patent and other intellectual property rights are, and may in the future be, subject to third party interests such as

co- ownership. If we are unable to obtain an exclusive license to such third- party co- owners' interest, in such patent and other intellectual property rights, such third- party co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. We or our licensors may need the cooperation of any such co- owners of our licensed patent and other intellectual property rights in order to enforce them against third parties, and such cooperation may not be provided to us or our licensors. Additionally, we may not have complete control over the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. It is possible that our licensors' filing, prosecution and maintenance of the licensed patents and patent applications, enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, and accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to file, prosecute, maintain, enforce and defend such patents and patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our technology and any product candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors or other third parties from making, using and selling competing products. Furthermore, our owned and in- licensed patent rights may be subject to a reservation of rights by one or more third parties. When new technologies are developed with government funding, in order to secure ownership of patent rights related to the technologies, the recipient of such funding is required to comply with certain government regulations, including timely disclosing the inventions claimed in such patent rights to the U. S. or foreign government and timely electing title to such inventions. A failure to meet these obligations may lead to a loss of rights or the unenforceability of relevant patents or patent applications. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting, maintaining, enforcing and defending patents and other intellectual property rights on our technology and our product candidates in all jurisdictions throughout the world would be prohibitively expensive, and accordingly, our intellectual property rights in some jurisdictions outside the U. S. could be less extensive than those in the U. S. In some cases, we or our licensors may not be able to obtain patent or other intellectual property protection for certain technology and product candidates outside the U. S. In addition, the laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as federal and state laws in the U. S. Consequently, we and our licensors may not be able to obtain issued patents or other intellectual property rights covering our product candidates and our technology in all jurisdictions outside the U. S. and, as a result, may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the U. S., or from selling or importing products made using our inventions in and into the U. S. or other jurisdictions. Third parties may use our technologies in jurisdictions where we and our licensors have not pursued and obtained patent or other intellectual property protection to develop their own products and, further, may export otherwise infringing, misappropriating or violating products to territories where we have patent or other intellectual property protection, but enforcement is not as strong as that in the U. S. These products may compete with our product candidates and our technology and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Additionally, many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain jurisdictions, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violation of our patent and other intellectual property rights or marketing of competing products in violation of our intellectual property rights generally. For example, an April 2019 report from the Office of the U. S. Trade Representative identified a number of countries, including China, Russia, Argentina, Chile and India, where challenges to the procurement and enforcement of patent rights have been reported. Proceedings to enforce our or our licensors' patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patent and other intellectual property rights at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We or our licensors may not prevail in any lawsuits that we or our licensors initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many jurisdictions have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many jurisdictions limit the enforceability of patents against government agencies or government contractors. In these jurisdictions, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. We may be involved in lawsuits to protect or enforce our patents or other intellectual property or the intellectual property of our licensors, which could be expensive, time-consuming, and unsuccessful. Competitors may infringe our patents or other intellectual property or the intellectual property of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time- consuming and divert the time and attention of our management and scientific personnel. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. In addition, in an infringement proceeding or a declaratory judgment action, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would

involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Changes in patent law in the U. S. or worldwide could diminish the value of patents in general, thereby impairing our ability to protect our product candidates and our technology. Changes in either the patent laws or interpretation of patent laws in the U. S. and worldwide, including patent reform legislation such as the Leahy- Smith America Invents Act ~~(~~**, or** Leahy- Smith Act ~~)~~, could increase the uncertainties and costs surrounding the prosecution of any owned or in- licensed patent applications and the maintenance, enforcement or defense of any current in- licensed issued patents and issued patents we may own or in- license in the future. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost- effective avenues for competitors to challenge the validity of patents, and enable third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO- administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the U. S., the first to invent the claimed invention was entitled to the patent, while outside the U. S., the first to file a patent application was entitled to the patent. After March 2013, under the Leahy- Smith Act, the U. S. transitioned to a first- to- file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our in- licensed issued patents and issued patents we may own or in- license in the future, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Since patent applications in the U. S. and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor' s patents or patent applications. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U. S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim unpatentable even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to review patentability of our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in- licensed patent applications and the enforcement or defense of our owned or in- licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. As one example, in the case Assoc. for Molecular Pathology v. Myriad Genetics, Inc., the U. S. Supreme Court held that certain claims to DNA molecules are not patentable simply because they have been isolated from surrounding material. Moreover, in 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to patent- ineligible subject matter. Accordingly, in view of the guidance memo, there can be no assurance that claims in our patent rights covering our product candidates or our technology will be held by the USPTO or equivalent foreign patent offices or by courts in the U. S. or in foreign jurisdictions to cover patentable subject matter. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U. S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and / or patent applications will be due to be paid to the USPTO and various government patent agencies outside of the U. S. over the lifetime of our owned or licensed patent rights. We rely on our outside counsel and other professionals or our licensing partners to pay these fees due to the USPTO and non- U. S. government patent agencies. The USPTO and various non- U. S. government patent agencies also require compliance with several procedural, documentary and other similar provisions during the patent application process. We rely on our outside counsel and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a

late fee or by other means in accordance with the applicable rules. There are situations, however, in which non- compliance can result in abandonment, loss of priority or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects. We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in- licenses. We currently have rights to certain intellectual property through the OUI / MRC License. Because our programs may require the use of additional intellectual property rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in- license or use these intellectual property rights. In addition, with respect to any patent or other intellectual property rights that we co- own with third parties, we may require exclusive licenses to such co- owners' interest in such patent or other intellectual property rights. However, we may be unable to secure such licenses or otherwise acquire or in- license any intellectual property rights related to compositions, methods of use, processes or other components from third parties that we identify as necessary for our product candidates and our technology on commercially reasonable terms, or at all. Even if we are able to in- license any such necessary intellectual property, it could be on non- exclusive terms, thereby giving our competitors and other third parties access to the same intellectual property licensed to us, and the applicable licensors could require us to make substantial licensing and royalty payments. The licensing or acquisition of third- party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third- party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment. We sometimes collaborate with non- profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to third parties, potentially blocking our ability to pursue our research program and develop and commercialize our product candidates. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have licensed, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects. Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the U. S. or abroad. Our owned and licensed patent rights may be subject to priority, validity, inventorship and enforceability disputes. If we or our licensors are unsuccessful in any of these proceedings, such patent rights may be narrowed, invalidated or held unenforceable, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or we may be required to cease the development, manufacture and commercialization of one or more of our product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. If we or one of our licensors initiate legal proceedings against a third party to enforce a patent covering our product candidates or our technology, the defendant could counterclaim that the patent covering the product candidate or technology is invalid or unenforceable. In patent litigation in the U. S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the U. S. or abroad, even outside the context of litigation. Such mechanisms include re- examination, interference proceedings, derivation proceedings, post grant review, inter partes review and equivalent proceedings such as opposition, invalidation and revocation proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates or our technology or prevent third parties from competing with our product candidates or our technology. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates or technology. Such a loss of patent protection could have a material adverse effect on our business, financial condition, results of operations and prospects. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know- how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the U. S. are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, contractors and other parties who have access to such technology and processes. However, we may not be able to prevent the unauthorized disclosure or use of our technical know- how or other trade secrets by the parties to these agreements. Monitoring unauthorized uses and

disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breach or violate the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets and third parties could use our trade secrets to compete with our product candidates and our technology. Additionally, we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems; however, such systems and security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors or other third parties. Competitors or third parties could purchase our product candidates or our technology and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our intellectual property rights or develop their own competitive technologies that fall outside the scope of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate such trade secrets, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, our business, financial condition, results of operations and prospects could be materially and adversely affected. Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could harm our business. Our commercial success depends upon our ability and the ability of our collaborators, if any, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may become party to, or be threatened with, adversarial proceedings or litigation in which third parties may assert infringement, misappropriation or other violation claims against us, alleging that our product candidates, manufacturing methods, formulations or administration methods are covered by their patents. Given the vast number of patents and other intellectual property in our field of technology, we cannot be certain or guarantee that we do not infringe, misappropriate or otherwise violate patents or other intellectual property. Other companies and institutions have filed, and continue to file, patent applications that may be related to our technology and, more broadly, to gene therapy and related manufacturing methods. Some of these patent applications have already been allowed or issued and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that we may be subject to claims of infringement of the patent rights of third parties. If a patent holder believes the manufacture, use, sale or importation of our product candidates or our technology infringes its patent, the patent holder may sue us even if we have licensed other patent rights for our technology. We are aware of certain patents in the U. S. and other jurisdictions owned by third parties that claim subject matter that relates to our product candidates and the EDO platform. Such third parties may assert these patents against us in litigation in the U. S. or other jurisdictions. The outcome of any such litigation is uncertain and, even if we prevail, the costs of such litigation could have a material adverse effect on our financial position, result in disclosure of our trade secrets, distract key personnel from the continued development of our business, and adversely affect our ability to enter or maintain commercial relationships with collaborators, clients or customers. If we are unsuccessful in such litigation, we could be prevented from commercializing products or could be required to take licenses from such third parties which may not be available on commercially reasonable terms, if at all. It is also possible that we have failed to identify relevant third- party patents or applications. Because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our product candidates or our technology and we may not be aware of such patents. Furthermore, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the U. S. may remain confidential until a patent issues. Moreover, it is difficult for industry participants, including us, to identify all third- party patent rights that may be relevant to our product candidates and our technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may incorrectly conclude that a third- party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third- party patents are valid, enforceable and infringed, which could adversely affect our ability to commercialize our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U. S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U. S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims

of any such U. S. patent. If we are found to infringe a third party' s valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non- exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects. Intellectual property litigation or other proceedings could cause us to spend substantial resources and distract our personnel from their normal responsibilities. Competitors may challenge the validity and enforceability of our patent rights or those of our licensing partners, infringe, misappropriate or otherwise violate our or our licensors' patent and other intellectual property rights, or we may be required to defend against claims of infringement, misappropriation or other violation. Litigation and other proceedings in connection with any of the foregoing claims can be unpredictable, expensive and time - consuming. Even if resolved in our favor, litigation or other proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our scientific, technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors or other third parties may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could adversely affect our ability to compete in the marketplace and could have a material adverse effect on our business, financial condition, results of operations and prospects. We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property. Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual' s current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or be required to obtain licenses to such intellectual property rights, which may not be available on commercially reasonable terms or at all. An inability to incorporate such intellectual property rights would harm our business and may prevent us from successfully commercializing our product candidates. In addition, we may lose personnel as a result of such claims and any such litigation , or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates and our technology, which would have a material adverse effect on our business, results of operations, financial condition and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our scientific and management personnel. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. Moreover, even when we obtain agreements assigning intellectual property to us, the assignment of intellectual property rights may not be self- executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have pre- existing or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. Disputes about the ownership of intellectual property that we own may have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, we or our licensors may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our owned or licensed patent rights. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and our product candidates. Such challenges may also result in our inability to develop, manufacture or commercialize our technology and product candidates without infringing third- party patent rights. In addition, if the breadth or strength of protection provided by our owned or licensed patent rights are threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technology and product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. If we do not obtain patent term extension for our product candidates, our business may be harmed. Under the ~~Drug Price Competition and Patent Term Restoration Act of 1984,~~

~~or the~~ Hatch- Waxman Amendments to the FDCA, a company may file an ~~abbreviated new drug application, or~~ ANDA ~~,~~ seeking approval of a generic version of an approved innovator product. Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates and our technology, one or more of our U. S. patents that we license or may own in the future may be eligible for limited patent term extension under Hatch- Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in- license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. We may be subject to claims challenging the inventorship or ownership of our patent and other intellectual property rights. We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in- licensed patent rights, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates or technology. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in- licensed patent rights, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of or right to use intellectual property that is important to our product candidates or our technology. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our current and future trademark applications in the U. S. and other foreign jurisdictions may not be allowed or may be subsequently opposed. Once filed and registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time- consuming, particularly for a company of our size. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects. Intellectual property rights do not necessarily address all potential threats. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make products that are similar to our product candidates but that are not covered by ~~the~~ intellectual property, including the claims of the patents, that we own or license currently or in the future; • we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or license currently or in the future; • we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating **,** or otherwise violating our owned or licensed intellectual property rights; • it is possible that our or our licensors' current or future pending patent applications will not lead to issued patents; • issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by third parties; • third parties might conduct research and development activities in jurisdictions where we do not have patent or other intellectual property rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • the patents or other intellectual property rights of others may have an adverse effect on our business; and • we may choose not to file a patent for certain trade secrets or know- how, and a third party may subsequently file a patent covering such intellectual property. Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor or other third party will discover our trade secrets or that our trade secrets will be misappropriated or disclosed. Because we currently rely on certain third parties to manufacture all or part of our product candidates and to perform quality testing, and

because we may need to collaborate with various third parties for the advancement of our product candidates and technology, we may be required to, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaboration agreements, services agreements, consulting agreements and other similar agreements prior to beginning research or disclosing any proprietary information to such third parties. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors or other third parties, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. 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 inside and outside the U. S. are less willing or unwilling to protect trade secrets. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third- party, we would have no right to prevent them from using that technology or information to compete with us. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets by third parties. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s or other third party' s discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may harm our business, financial condition, results of operations and prospects. Risks Related to Employee Matters, Managing Growth and Other Operational Matters Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel. We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment **agreements** ~~offer letters~~ with our executive officers, each of them may terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited. We expect to expand our headcount to support our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. As of December 31, ~~2023~~ **2024** , we had ~~64~~ **81** full- time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate receives marketing approval, sales, marketing, distribution and coverage and reimbursement capabilities. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, ~~expand our facilities~~ and continue to recruit and train additional qualified personnel **and may need to expand our facilities** . Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. As a growing biotechnology company, we expect to pursue new platforms and product candidates in ~~multiple~~ **several** therapeutic areas and across a ~~wide~~ range of diseases. Successfully developing product candidates for, and fully understanding the regulatory and manufacturing pathways to, each of these therapeutic areas and disease states requires a significant depth of talent, resources and corporate processes in order to allow simultaneous execution across multiple areas. Due to our limited resources, we may not be able to effectively manage this simultaneous execution and the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, legal or regulatory compliance failures, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively and commercialize our

product candidates, if approved, will depend in part on our ability to effectively manage the future development and expansion of our company. Our international activities subject us to various risks, and our failure to manage these risks could adversely affect our results of operations. We face significant operational risks as a result of doing business internationally, such as: • fluctuations in foreign currency exchange rates; • differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls; • potentially adverse and / or unexpected tax consequences, including penalties due to the challenge by tax authorities on our tax position; • potential changes to the accounting standards, which may influence our financial situation and results; • compliance with tax, employment, immigration and labor laws should we have any employees living or traveling abroad; • becoming subject to the different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties; • reduced protection of, or significant difficulties in enforcing, intellectual property rights, or increased risk of intellectual property disputes, in certain countries; • difficulties in attracting and retaining qualified consultants, contractors, and personnel; • restrictions imposed by any applicable local labor practices and laws on our business and operations, including unilateral cancellation or modification of contracts; • rapid changes in global government, economic and political policies and conditions, political or civil unrest or instability, terrorism or epidemics and other similar outbreaks or events, and potential failure in confidence of our suppliers or customers due to such changes or events; • geopolitical tensions that affect our activities, operations and / or operations of our contractors, consultants, collaborators, vendors or partners; and • tariffs, trade protection measures, import or export licensing requirements, trade embargoes and other trade barriers. Future acquisitions or strategic alliances could disrupt our business and harm our financial condition and results of operations. We may acquire additional businesses, technologies or assets, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products or product candidates resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions, include: • diversion of management time and focus from operating our business to addressing acquisition integration challenges; • coordination of research and development efforts; • retention of key employees from the acquired company; • changes in relationships with collaborators as a result of product acquisitions or strategic positioning resulting from the acquisition; • cultural challenges associated with integrating employees from the acquired company into our organization; • the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies; • liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities; • unanticipated write- offs or charges; and • litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties. Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations. Our internal information technology systems, or those of our vendors, collaborators or other contractors or consultants, may fail or suffer **from cyber** security **incidents or** breaches, loss or leakage of data and other disruptions or compromise, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, or trigger contractual and legal obligations, potentially exposing us to liability, reputational harm or otherwise adversely affecting our business and financial results. We are increasingly dependent upon information technology systems and infrastructure to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we, our vendors, collaborators and other contractors or consultants, do so in a secure manner to maintain the availability, security, confidentiality, privacy and integrity of such confidential information. Despite the implementation of security measures, given the size and complexity of our internal information technology systems and those of our current and future vendors, collaborators and other contractors or consultants, and the increasing amounts of confidential information that we and our affiliated third parties maintain, such information technology systems are still vulnerable to damage or interruption from computer viruses, computer hackers, malicious code, **ransomware, social engineering attacks (including phishing attacks),** employee error, theft or misuse, denial- of- service attacks, sophisticated nation- state and nation- state- supported actors, unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures or other compromise. The risk of a ~~security~~ **cybersecurity incident,** breach or disruption, particularly through cyber- attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. As a result of the effects of a pandemic, such as the COVID- 19 pandemic or other health crisis, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely for a portion of their time, which may create additional opportunities for cybercriminals to exploit vulnerabilities. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. As such, we may experience ~~security~~ **cybersecurity incidents,** breaches **, or compromises** that may remain undetected for an extended period. We may be unable to anticipate all types of ~~security~~ **cybersecurity** threats, or implement preventive measures effective against all such ~~security~~ **cybersecurity**

threats. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection and to remove or obfuscate forensic evidence. We and certain of our service providers are from time to time subject to cyberattacks and ~~security~~ **cybersecurity** incidents **, breaches, or compromises** . While we do not believe that we have experienced any significant system failure, accident or ~~security~~ **cybersecurity** breach **or incident** to date, if such an event were to occur, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary or confidential information or other disruptions. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we were to experience a significant cybersecurity **incident or** breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the **incident or** breach to counterparties, data subjects, regulators or others could be material. In addition, our remediation efforts may not be successful. Moreover, if the information technology systems of our vendors, collaborators and other contractors and consultants become subject to disruptions or ~~security~~ **cybersecurity incidents or** breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information. To the extent that any disruption ~~or~~ **,** ~~security~~ **cybersecurity incident,** breach **, or compromise** were to result in a loss of, or damage to, our or our vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including litigation exposure and penalties and fines. Any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our customers or employees, could harm our reputation, compel us to comply with federal and / or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. We could become the subject of regulatory action or investigation, and our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed. As a result of such an event, we may also be in breach of our contractual obligations. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects. The financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we maintain. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above. Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a natural disaster, pandemic or other catastrophic event. We depend on our employees, consultants, CDMOs and CROs, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions we take for natural disasters or other catastrophic events, these events, including terrorist attack, pandemics, hurricanes, fire, floods and ice and snowstorms, could result in significant disruptions to our research and development, preclinical studies, clinical trials, and, ultimately, commercialization of our products. Long- term disruptions in the infrastructure caused by events, such as natural disasters, the outbreak of war, the escalation of hostilities and acts of terrorism or other " acts of God, " particularly involving cities in which we have offices, manufacturing or clinical trial sites, could adversely affect our businesses. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not respond or be adequate to compensate us for all losses that may occur. Any natural disaster or catastrophic event affecting us, our CDMOs, CROs, regulatory agencies or other parties with which we are engaged could have a significant negative impact on our operations and financial performance. Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non- performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and ~~its~~ **our** financial condition and results of operations. 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. Although we are not a borrower or party to any such instruments with any financial institution that has experienced such events, if we were to borrow money in the future and if any of our lenders or counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds. In addition, if any of our customers, suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay or perform their obligations to us or to enter into new commercial arrangements requiring additional payments to us or additional funding could be adversely affected. In this regard, counterparties to credit agreements and arrangements with banks in receivership or other financial difficulty, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure or reorganization of such financial institutions and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008- 2010 financial crisis. Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U. S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $ 25 billion of loans to financial institutions secured by certain government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread

demands for customer withdrawals or other liquidity needs of financial institutions for immediate liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions in the future, or that they would do so in a timely fashion. 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 financial arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. In addition, investor concerns regarding the U. S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and / or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity, our current and / or projected business operations, and financial condition and results of operations. The effects of the COVID- 19 pandemic, or a future pandemic, epidemic or outbreak of an infectious or highly contagious disease, may materially and adversely affect our business and financial results and could cause a disruption in the development of our product candidates. Public health crises such as pandemics, including the COVID- 19 pandemic or similar outbreaks, could adversely impact our business. For example, in connection with COVID- 19, we and our CDMOs and CROs have in the past experienced a reduction in the capacity to undertake research- scale production and to execute some preclinical studies, and we may face future similar disruptions that affect our ability to initiate and complete preclinical studies. We may also encounter disruptions in procuring items that are essential for our research and development activities, such as raw materials used in the manufacture of any product candidates, laboratory supplies used in our preclinical and clinical studies, or animals that are used for preclinical testing for which there are or may be shortages because of ongoing efforts to address COVID- 19 or a future health pandemic. The ultimate extent to which COVID- 19, or a future outbreak of other highly infectious or contagious diseases, impacts our operations or those of our third- party partners, including our preclinical studies or clinical trial operations, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope, severity and duration of an outbreak, actions taken to contain an outbreak or mitigate its impact, and the direct and indirect economic effects of an outbreak and containment measures, among other developments. Risks Related to Ownership of Our Common Stock The stock price of our common stock has been and may continue to be volatile or may decline regardless of our operating performance and prospects. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. An active or liquid market in our common stock may not develop or, if it does develop, it may not be sustainable, and the prices at which shares of our common stock trade in the market have fluctuated **considerably** and may fluctuate in the future considerably or decline or be quite volatile regardless of our operating performance and prospects. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price or the per share price you paid for your shares. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and / or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. In February 2024, we sold shares **of our common stock** under our ATM program and in the Follow- on Offering, receiving ~~in~~ aggregate net proceeds of $ 86. ~~8~~ **3** million after deducting underwriters' fees and ~~before deducting~~ costs of the offerings. Any debt financing or preferred equity financing, if available, may involve, agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we may be required to delay, limit, reduce or eliminate some or all of our research and development programs, pipeline expansion or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If securities or industry analysts do not continue to publish research or reports or publish inaccurate or unfavorable research or reports about our business, our stock price and trading volume could decline. The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. In the event one or more analysts downgrade our stock price or change their opinion of our stock price, our stock price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline. The price of our common

stock is volatile and fluctuates substantially, which could result in substantial losses for holders of our common stock. The stock market in general, and the market for smaller biopharmaceutical companies in particular, have experienced extreme price volatility and volume fluctuations that have often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price you paid for it. The market price for our common stock may be influenced by many factors, including: • timing and results of, or developments in, preclinical studies and clinical trials of our product candidates or those of our competitors or potential competitors; • adverse regulatory rulemaking, guidance or decisions, including failure to receive marketing approvals for our product candidates; • our success in commercializing any product candidates that may be approved; • the success of competitive products or technologies; • regulatory or legal developments in the U. S. and other countries; • developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to our product candidates; • the results of our efforts to discover, develop, acquire or in- license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies; • actual or anticipated changes in estimates as to our financial condition or results, clinical outcomes, development timelines or recommendations by securities analysts; • variations in our financial condition or results or the financial condition or results of companies that are perceived to be similar to us; • sales of our common stock by us, our executive officers, directors or principal stockholders or others; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry, political and market conditions, including conditions resulting from the effects of the COVID- 19 pandemic, high inflation and capital market disruptions, and government macroeconomic policies; and • the other factors described in this " Risk factors " section. Any of the factors listed above could materially adversely affect your investment in our common stock, and our common stock may trade at prices significantly below the price you paid for our stock, which could contribute to a loss of all or part of your investment. In such circumstances the trading price of our common stock may not recover and may experience a further decline. In the past, following periods of volatility in the market price of a company' s securities, securities class- action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and maintain liability insurance coverages and may also result in the diversion of management' s attention and resources. Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn resulting from the effects of the COVID- 19 pandemic or future pandemic could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. In addition, the current military conflict between Russia and Ukraine ~~and ,~~ armed conflict in Israel and the Gaza Strip **and military action in other parts of the Middle East** could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, **import /** export controls or other actions that have been or may be initiated by nations, including the U. S. or the EU **, including previously pending legislative proposals in the U. S. relating to China and certain biotechnology companies of concern** , or actions taken by Russia (e. g., potential cyberattacks, disruption of energy flows, etc.) could adversely affect our business and / or our supply chain, our CROs, CDMOs and other third parties with which we conduct business. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could impair our ability to achieve our growth strategy, could harm our financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that our current or future service providers, manufacturers or other collaborators may not survive such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. We cannot anticipate all of the ways in which the current economic climate, including increasing interest rates and high inflation, and financial market conditions could adversely impact our business. Our executive officers, directors and principal shareholders, if they choose to act together, will continue to have the ability to significantly influence all matters submitted to stockholders for approval. Based upon our common stock outstanding as of ~~March 1~~ **December 31** , 2024, our executive officers, directors, greater than five percent shareholders and their affiliates beneficially own approximately ~~47~~ **51** . ~~1~~ **9** % of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs, even though some of these persons or entities may have interests that are different than those of yours. For example, these stockholders, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of substantially all of our assets. This concentration of ownership may: • delay, defer or prevent a merger, consolidation or sale of all or substantially all of our assets that may be desired by other stockholders; • delay, defer or prevent a change in control transaction involving us that other stockholders may desire; or • entrench our management and board of directors. Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. The sale of a significant number of shares of our common stock, or the perception that such sales could occur, could cause the market price of our common stock to drop significantly, even if our business is

doing well. Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock, impair our ability to raise capital through the sale of additional equity securities, and make it more difficult for you to sell your common stock at a time and price that you deem appropriate. In addition, holders of an aggregate of 8, 778, 170 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also filed ~~a~~ **or will file** registration ~~statement~~ **statements** on Form S- 8 to register all of the shares of common stock that we are able to issue under our equity compensation plans. Shares registered under these registration statements on Form S- 8 can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, vesting arrangements, exercise of options and any contractual restrictions that may apply to such shares. We are an " emerging growth company " and a " smaller reporting company, " and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors. We are an " emerging growth company, " or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. We may remain an EGC until the end of the year that is the fifth anniversary of the closing of our IPO, although if the market value of our common stock that is held by non- affiliates exceeds $ 700. 0 million as of any June 30 before that time or if we have annual gross revenues of $ 1. 235 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $ 1. 0 billion of non- convertible debt over a three- year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include: • not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting; • not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements; • reduced disclosure obligations regarding executive compensation; and • exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. Even after we no longer qualify as an EGC, we may continue to qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation. In addition, if we are a smaller reporting company with less than $ 100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act of 2002 ~~(~~**, or** Section 404 ~~)~~. In reliance on these exemptions, we have taken advantage of reduced reporting obligations in this 10- K. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either irrevocably elect to " opt out " of such extended transition period or no longer qualify as an EGC. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies. We incur substantial costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices. As a public company, and even more so after we are no longer an EGC or a smaller reporting company, we incur or will incur significant legal, accounting and other expenses. The Sarbanes- Oxley Act of 2002, the Dodd- Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and may continue to increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements and have made and will make some activities more time- consuming and costly compared to when we were a private company. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we may incur as a public company or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management' s time and attention from revenue- generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed. Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting beginning with this 10- K. However, while we remain an EGC or a smaller reporting company with less than $ 100 million in annual revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered

public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, engaging outside consultants and adopting a detailed work plan to assess and document the adequacy of internal control over financial reporting, continuing steps to improve control processes as appropriate, validating through testing that controls are functioning as documented and implementing a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements, particularly if such material weakness results in the necessity of a restatement of our historical financial statements. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our stock. We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an EGC under the JOBS Act or a smaller reporting company with less than $ 100 million in annual revenue, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five fiscal years after our IPO, which occurred on May 6, 2022. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management' s assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation, which could have a negative effect on the trading price of our stock. Anti- takeover provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management. Anti- takeover provisions in our **third** amended and restated certificate of incorporation and our **second** amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions: • establish a classified board of directors such that only one of three classes of directors is elected each year; • allow the authorized number of our directors to be changed only by resolution of our board of directors; • limit the manner in which stockholders can remove directors from our board of directors; • establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors; • require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent; • limit who may call stockholder meetings; • authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a " poison pill " that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and • require the approval of the holders of at least 66. 7 % of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law ~~(~~**, or** DGCL ~~)~~, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Our **second** amended and restated bylaws designate the Court of Chancery of the State of Delaware and the federal district courts of the United States of America as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers and employees. Our **second** amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: • any derivative action or proceeding brought on our behalf; • any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders; • any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or • any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time)

or governed by the internal affairs doctrine. These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act **,** creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our **second** amended and **restated** bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our **second** amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find the exclusive forum provision contained in our **second** amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and operating results. We may not be able to continue to satisfy listing requirements of the Nasdaq Global Select Market or maintain a listing of our common stock on the Nasdaq Global Select Market. Our common stock is listed on the Nasdaq Global Select Market. We must meet certain financial and liquidity criteria to maintain such listing. If we violate or fail to meet any of the Nasdaq Global Select Market ' s listing standards, our common stock may be delisted. In addition, our board of directors may determine that the cost of maintaining our listing on a national securities exchange outweighs the benefits of such listing. A delisting of our common stock from the Nasdaq Global Select Market may materially impair our stockholders' ability to buy and sell our common stock and could have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock. The delisting of our common stock could significantly impair our ability to raise capital and the value of your investment. General Risk Factors Changes in tax laws or regulations or in their implementation or interpretation may adversely affect our business and financial condition. New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business or financial condition. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. A number of other factors could materially adversely affect our business and financial condition including: tax policy initiatives and reforms under consideration (such as those related to the Organization for Economic Co- Operation and Development' s ~~(~~**, or** OECD ~~)~~, Base Erosion and Profit Shifting ~~(~~**, or** BEPS ~~)~~, Project, the European Commission' s state aid investigations and other initiatives), the practices of tax authorities in jurisdictions in which we operate; the resolution of issues arising from tax audits or examinations and any related interest or penalties. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. The ~~Organization for Economic Co- operation & Development, or~~ OECD ~~,~~ Pillar Two Model Rules established a minimum global effective tax rate of 15 % on country- by- country basis. EU member states along with many other countries adopted or expected to adopt the OECD Pillar Two Model effective January 1, 2024 or thereafter. The OECD and other countries continue to publish guidelines and legislation which include transition and safe harbor rules. We continue to monitor new legislative changes and assess the global impact of the Pillar Two Model Rules. Based on our initial assessment, we anticipate Pillar Two top- up taxes to be immaterial. The U. S. government may enact significant new changes to the taxation of business entities including, among others, an increase in the corporate income tax rate. Furthermore, the rules dealing with U. S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service **, or IRS,** and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices in jurisdictions in which we operate, could increase the estimated tax liability that we have expensed to date and paid or accrued on our balance sheets, and otherwise affect our financial position, future results of operations, cash flows in a particular period and overall or effective tax rates in the future in countries where we have operations, reduce post- tax returns to our shareholders and increase the complexity, burden and cost of tax compliance. Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an unforeseen manner, resulting in unanticipated costs, taxes or non- realization of expected benefits. A tax authority may disagree with tax positions that we take, which could result in increased tax liabilities. For example, His Majesty' s Revenue & Customs, the IRS or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a " permanent establishment " under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if

we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable. Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be subject to limitations. We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating losses, or NOLs, or research and development tax credit carryforwards. As of December 31, ~~2023~~ **2024**, we had federal **NOLs of $ 58. 2 million** and state NOL carryforwards of $ ~~23~~ **76**. ~~4~~ **6** million. We did not generate U. K. NOLs in ~~2022~~ **2024** ~~or 2023~~, and do not anticipate any going forward **as our U. K. entity, PepGen Limited, was dissolved on December 10, 2024**. As a company that carries out extensive research and development activities, we sought to benefit from the U. K. research and development tax relief programs, being the Small and Medium- sized Enterprises R & D tax relief program ~~(~~**, or** SME Program ~~)~~, and, to the extent that our projects are grant funded or relate to work subcontracted to the company by third parties, the Research and Development Expenditure Credit program ~~(~~**, or** RDEC Program ~~)~~. Under the SME Program, we may be able to surrender the trading losses that arise from our qualifying research and development activities for a cash rebate of approximately 33. 4 % of the surrenderable losses. The majority of our research and development activities during 2021 were eligible for inclusion within these tax credit cash rebate claims. We may not be able to continue to claim payable research and development tax credits in the future if we cease to qualify as an SME, based on size criteria concerning employee headcount, turnover and gross assets or if we no longer conduct qualifying research and development activities through our wholly- owned subsidiary PepGen Limited. The U. K. Finance Act of 2021 introduced a cap on payable credit claims under the SME Program in excess of £ 20, 000 with effect from April 2021 by reference to, broadly, three times the total PAYE and NICs liability of the company, subject to an exception which prevents the cap from applying. That exception requires the company to be creating, taking steps to create or managing intellectual property, as well as having qualifying research and development expenditure in respect of connected parties which does not exceed 15 % of the total qualifying expenditure. If such exception does not apply, this could restrict the amount of credit that we are able to claim. For the year ended December 31, ~~2023~~ **2024**, our research and development tax credits from the U. K. government were not material as the intellectual property was transferred from our wholly- owned U. K. subsidiary, PepGen Limited, to the parent company, PepGen Inc. in January 2022. For U. S. federal income tax purposes, in general, under Sections 382 and 383 of the U. S. Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an " ownership change, " generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three- year period, is subject to limitations on its ability to utilize its pre- change NOLs and pre- change research and development tax credit carryforwards to offset post- change income or taxes. We have not conducted a study to assess whether any such ownership changes have occurred. We may experience such ownership changes in the future. As a result, if, and to the extent that, we earn net taxable income, our ability to use our NOL carryforwards and research and development tax credit carryforwards to offset such taxable income may be subject to limitations. Additionally, the use of the U. K. NOL carryforwards could be restricted, under Part 14 of the Corporation Tax Act 2010, if a " change in ownership " of either PepGen Inc. or PepGen Limited were to occur and certain other conditions are met. A " change in ownership " is defined, broadly, as the acquisition by one or more persons of more than half of the ordinary share capital of a company. The use of the U. K. NOL carryforwards could be restricted if, within a certain period of a change in ownership, there is a major change in the conduct of PepGen Limited' s trade, PepGen Limited' s trading activities become small or negligible, or if certain other conditions are met. Any restructuring or change in the nature of our operations of our company may give rise to tax liabilities and / or restrictions in the amount and / or availability of tax attributes. We have undergone, and may in the future undertake, changes in the nature or conduct of our operations. For example, pursuant to an asset transfer agreement effective as of January 1, 2022, we effected a novation of all intellectual property assets of our wholly- owned U. K. subsidiary PepGen Limited to PepGen Inc., which resulted in the recording of a tax charge of $ 3. 7 million, including $ 0. 7 million related to an uncertain tax position. **PepGen Limited was dissolved on December 10, 2024 and we recognized a $ 0. 7 million tax benefit associated with the resolution of the uncertain tax position.** Any future actions regarding transfer of assets from our U. K. subsidiary or other **potential** international subsidiaries could give rise to tax liabilities for us and / or to the erosion of our tax attributes (such as **NOLs** ~~net operating losses~~). Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We are subject to certain reporting requirements of the ~~Securities~~ Exchange Act ~~of 1934, as amended, (Exchange Act)~~. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected. As a public company, we may be at an increased risk of securities class action litigation. Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. We may be exposed to significant foreign exchange risk. We incur portions of our expenses, and may in the future derive revenues, in a variety of currencies. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. Fluctuations in currency exchange rates have had, and will continue to have, an impact on our

results as expressed in U. S. dollars. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows. **97**