

Risk Factors Comparison 2024-02-29 to 2023-03-15 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this ~~Quarterly~~ **Annual** Report on Form 10-~~Q-K~~, including our financial statements and the related notes and the section of this ~~Quarterly~~ **Annual** Report on Form 10-~~Q-K~~ titled “ Management’ s Discussion and Analysis of Financial Condition and Results of Operations, ” before deciding whether to invest in our common stock. If any of the following risks actually occur, our business, reputation, financial condition, results of operations, revenue and future prospects could be seriously harmed. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that adversely affect our business. Unless otherwise indicated, references to our business being seriously harmed in these risk factors and elsewhere will include harm to our business, reputation, financial condition, results of operations, future prospects and stock price. If our business is seriously harmed, the market price of our common stock could decline, and you could lose part or all of your investment. Risk Factor Summary Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. The following is a summary of the principal risks that could seriously harm our business, all of which are more fully described below. This summary should be read in conjunction with the other risk factors included in this “ Risk Factors ” section and should not be relied upon as an exhaustive summary of the material risks facing our business.

- We are in the early stages of drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.
- We have had recurring net losses, and we expect to continue to incur significant net losses for the foreseeable future.
- We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and / or eliminate one or more of our research and drug development programs or future commercialization efforts.
- All of our product candidates are based on a novel AAV genetic medicine technology with which there is limited regulatory and clinical experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. Further, the regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities.
- Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products or otherwise seriously harm our business.
- Adverse public perception or regulatory scrutiny of genetic medicine technology may negatively impact the developmental progress or commercial success of products that we develop alone or with collaborators.
- Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.
- The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, expensive, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.
- Our employees, independent contractors, consultants, research or commercial partners or collaborators and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies.
- Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors. Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements We are a clinical- stage genetic medicine company pioneering the development of product candidates using our targeted and evolved AAV vectors. We commenced operations in September 2013, have no products approved for commercial sale and have not generated any product revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. If our product candidates are not successfully developed and approved, we may never generate any product revenue. To date, we have not completed any clinical trials (including any pivotal clinical trial), obtained marketing approval for any product candidates, manufactured commercial scale quantities of any of our product candidates or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our limited operating history as a company and early stage of drug development make any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early- stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will be seriously harmed. We have incurred recurring net losses, including net losses of \$ **100.8 million and \$ 107.5 million** and \$ **71.3 million** for the years ended December 31, **2023 and 2022** and ~~2021~~, respectively. As of December 31, ~~2022~~ **2023**, we had an accumulated deficit of \$ **314.415** ~~5.3~~ million. We have devoted substantially all of our financial resources and efforts on research and development activities, including for our product candidates and our Therapeutic Vector Evolution platform. We do not expect to generate revenue from product sales for several years, if at all. We continue to incur significant research and development and other expenses related to our ongoing operations. The amount of our future net losses will depend, in part, on the level of our future expenditures and our ability to generate revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We

anticipate that our expenses will increase substantially if and as we: • progress our current and any future product candidates through preclinical and clinical development ; ~~• experience delays in our preclinical studies and clinical trials, whether current or planned, due to the novel coronavirus (“ COVID- 19 ”) pandemic, or other factors~~; • expand our manufacturing facilities and work with our contract manufacturers to scale up the manufacturing processes for our product candidates; • continue our research and discovery activities; • continue the development of our Therapeutic Vector Evolution platform; • initiate and conduct additional preclinical, clinical or other studies for our product candidates; • change or add additional contract manufacturers or suppliers; • seek regulatory approvals and marketing authorizations for our product candidates; • establish sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval; • acquire or in-license product candidates, intellectual property and technologies; • make milestone, royalty or other payments due under any current or future collaboration or license agreements; • obtain, maintain, expand, protect and enforce our intellectual property portfolio; • attract, hire and retain qualified personnel; • experience any delays or encounter other issues related to our operations; • meet the requirements and demands of being a public company; • are adversely impacted by general economic conditions, such as rising inflation and increased interest rates; • defend against any product liability claims or other lawsuits related to our products; and • ~~address~~ **experience delays in our preclinical studies and clinical trials, whether current or planned, due to the impact of the novel coronavirus (“ COVID- 19 ”) pandemic or , which may exacerbate the other magnitude of the factors discussed above similar pandemics or public health emergencies**. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders’ deficit and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline. Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time consuming, expensive and uncertain process that takes years to complete. Our operations have required substantial amounts of cash since inception. To date, we have financed our operations primarily through the sale of equity securities and to a lesser extent from cash received pursuant to our collaboration and license agreements. We have initiated clinical trials, which are ongoing, and have additional product candidates in preclinical development that may enter clinical development. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early stage research projects, continue preclinical and clinical development of our product candidates and, in particular, advance our product candidates through clinical trials. Even if we are successful in developing our product candidates, obtaining regulatory approvals and launching and commercializing any product candidate will require substantial funding. As of December 31, ~~2022~~ **2023**, we had \$ ~~218-299~~ **5-2** million in cash and cash equivalents and marketable securities. Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities will allow us to fund our planned operations for at least one year from the date of the issuance of the financial statements included in this Annual Report on Form 10- K. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. Our ability to raise additional capital may be adversely impacted if global economic conditions continue to worsen ~~or if as a result of volatility in credit and financial markets (including due to the residual effects of the COVID- 19 pandemic)~~; ~~including the spread of any variant thereof, causes new disruptions and volatility to credit and financial markets~~ and to product supply chains. If adequate funds are not available to us on a timely basis, we may be required to: • delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities or eliminate one or more of our development programs altogether; or • delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, or reduce our flexibility in developing or maintaining our sales and marketing strategy. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to, or jointly own some aspects of, our product candidates or technologies that we would otherwise pursue on our own. We do not expect to realize revenue from sales of products or royalties from licensed products in the foreseeable future, if at all, and unless and until a product candidate is clinically tested, approved for commercialization and successfully marketed. We will be required to seek additional funding in the future and currently intend to do so through collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution, and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives. Any of the above events could seriously harm our business and cause the price of our common stock to decline. Due to the significant resources required for the development of our product candidates, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on product candidates that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Due to the significant resources required for the development of our product candidates, in particular our product candidates in IND- enabling studies and those in clinical trials, we must decide which product candidates and indications to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential

decisions to delay, terminate or collaborate with third parties in respect of certain product candidates may subsequently also prove to be less than optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the biopharmaceutical industry, in particular for ophthalmology, cardiology and pulmonology, **and cardiology** diseases, our business could be seriously harmed. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights. The amount of our future losses is uncertain and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control and may be difficult to predict, including: • the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or collaboration partners; • the timing and cost of, and level of investment in research, development and commercialization activities, which may change from time to time; • the timing of receipt of approvals from regulatory authorities in the United States and internationally; • the timing and status of enrollment and safety and efficacy readouts for our clinical trials; • the cost of manufacturing, as well as building out our supply chain, which may vary depending on the quantity of production, the cost of continuing to establish and scale up our internal manufacturing capabilities, and the terms of any agreements we enter into with third-party suppliers; • timing and amount of any option, milestone, royalty or other payments due under any current or future collaboration or license agreement; • coverage and reimbursement policies with respect to our genetic medicine product candidates and potential future drugs that compete with our products, if approved; • expenditures that we may incur to acquire, develop or commercialize additional products and technologies; • the level of demand for our genetic medicine products, if approved, which may vary significantly over time; • future accounting pronouncements or changes in our accounting policies; and • the impact from general macroeconomic trends, such as higher inflation and increased interest rates. For example, most of our collaboration and license revenue for the year ended December 31, 2021 was from Roche. However, Roche terminated its collaboration and license agreement with us effective September 16, 2021. **Furthermore, most of our collaboration and license revenue for the year ended December 31, 2023 was from Astellas.** The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of financial analysts or investors for any period. If our revenue or operating results fall below or if operating expenses or other costs are higher than the expectations of analysts or investors or below or above, as the case may be, any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Risks Related to the Research, Discovery, Development and Commercialization of Our Product Candidates All of our product candidates are based on genetic medicine technology, and our future success depends on the successful development of this novel therapeutic approach. We cannot assure you that any development problems we or other genetic medicine companies experience in the future related to genetic medicine technology will not cause significant delays or unanticipated costs in the development of our product candidates, or that such development problems can be solved. In addition, the clinical study requirements of the **U. S. Food and Drug Administration (“FDA”)** and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities. Further, as we are developing novel treatments for diseases in which there is limited clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, European Medicines Agency (“EMA”) or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, few genetic medicine products have been approved by the FDA or comparable foreign regulatory authorities, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union or other jurisdictions. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval. Regulatory requirements governing genetic medicine products have evolved and may continue to change in the future. For example, the FDA has established the Office of Therapeutic Products within its Center for Biologics Evaluation and Research (“CBER”) to consolidate the review of genetic medicine and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. The National Institutes of Health (“NIH”) Guidelines for Research Involving Recombinant DNA Molecules (“NIH Guidelines”) require supervision of human gene transfer trials, including evaluation and assessment by an Institutional Biosafety Committee (“IBC”), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any

potential risk to the public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. We are subject to significant regulatory oversight by the FDA, and, in addition, the applicable IBC and Institutional Review Board (“ IRB ”), of each institution at which we or our collaborators conduct clinical trials of our product candidates, or a central IRB if appropriate, need to review and approve the proposed clinical trial. Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for genetic medicine products and require that we comply with these new guidelines. Changes in applicable regulatory guidelines may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all and could seriously harm our business. Adverse public perception or regulatory scrutiny of genetic medicine technology may negatively impact the developmental progress or commercial success of product candidates that we develop alone or with collaborators. The developmental and commercial success of our current product candidates, or any that we develop alone or with collaborators in the future, will depend in part on public acceptance of the use of genetic medicine technology, including the use of AAVs, for the prevention or treatment of human diseases. Adverse public perception of gene therapies may negatively impact our ability to raise capital or enter into strategic agreements for the development of product candidates. Genetic medicine remains a novel technology. The commercial success of our genetic medicine product candidates, if successfully developed and approved, may be adversely affected by claims that genetic medicine is unsafe, unethical or immoral. This may lead to unfavorable public perception and the inability of any of our product candidates to gain the acceptance of the public or the medical community. Unfavorable public perceptions may also adversely impact our or our collaborators’ ability to enroll clinical trials for our product candidates. Moreover, success in commercializing any product candidates that receive regulatory approval will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of such product candidates in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. Publicity of any adverse events in, or unfavorable results of, preclinical studies or clinical trials for any current or future product candidates, or with respect to the studies or trials of our competitors or of academic researchers utilizing similar technologies, even if not ultimately attributable to our technology or product candidates, could negatively influence public opinion. Negative public perception about the use of AAV technology in human therapeutics, whether related to our technology or a competitor’ s technology, could result in increased governmental regulation, delays in the development and commercialization of product candidates or decreased demand for the resulting products, any of which may seriously harm our business. Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences. Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Less common adverse effects may not become evident until investigational products are tested in large- scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If any serious adverse events occur, clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business could be seriously harmed. Treatment- related side effects could also affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us or our collaborators to cease further development of, deny approval of, or require us to cease selling any product candidates or products for any or all targeted indications. If we or our collaborators elect, or are required, to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated. Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to: • regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution; • regulatory authorities may require additional warnings on the label including “ boxed ” warnings, 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 create a Risk Evaluation and Mitigation Strategy (“ REMS ”), which could include a medication guide outlining the risks of such side effects for distribution to patients,

a communication plan for healthcare providers and / or other elements to assure safe use; • the product may become less competitive; • 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; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have no products approved for commercial sale, and we have never generated any revenue from product sales, and we may never generate product revenue or be profitable. We have no products approved for commercial sale and have not generated any revenue from product sales. We do not anticipate generating any revenue from product sales until after we have successfully completed clinical development and received regulatory approval for the commercial sale of a product candidate, which will not occur for several years, if ever. Our ability to generate revenue and achieve profitability depends significantly on many factors, including: • successfully completing research and preclinical and clinical development of our product candidates; • ~~the COVID-19 pandemic, which has resulted in, and in the future may continue to result in delays to patient enrollment, patients discontinuing their treatment or follow up visits or changes to trial protocols;~~ • obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials; • developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and any commercial demand for our product candidates; • identifying, assessing, acquiring and / or developing new product candidates; • negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; • the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future approved products, if any; • launching and successfully commercializing product candidates for which we obtain marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure; • obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our product candidates are commercialized; • obtaining adequate reimbursement for our product candidates or procedures using our product candidates from payors; • the convenience and durability of our treatment or dosing regimen; • acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidates, or any future product candidates, if approved, including relative to alternative and competing treatments; • patient demand for any of our product candidates that may be approved; • **addressing any competing technological and market developments; • the effects of any public health emergencies, including the COVID-19 pandemic, which may result in delays to patient enrollment, patients discontinuing their treatment or follow up visits or changes to trial protocols;** • maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and • attracting, hiring and retaining qualified personnel. Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts. Even if we are able to generate revenue from the sale of any approved products, we may not become profitable, and we will need to obtain additional funding through one or more equity or debt financings in order to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained 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 get reimbursement at any price and whether we own the commercial rights for that territory. If the number of addressable patients is not as large as we anticipate, the indication approved by regulatory authorities is narrower than we expect, the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines or the price and available third-party reimbursement are lower than anticipated, we may not generate significant revenue from sales of such product candidate, 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 would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock, all or any of which may **seriously harm our business. Public health..... condition and results of operations and could** seriously harm our business. We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all. Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be initiated or conducted as planned or completed on schedule, if at all. We also cannot be sure that submission of an IND or a clinical trial application ("CTA") will result in the FDA or other regulatory authority, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could delay, suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include: • inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials; • delays in reaching a consensus with regulatory agencies on study design or implementation of the clinical trials; • ~~adverse impacts from the COVID-19 pandemic as further described elsewhere in these risk factors;~~ • delays or failure in obtaining regulatory authorization to commence a trial; • delays in reaching agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • refusal of the FDA to accept data from clinical trials in geographies outside the United States; • delays in identifying, recruiting and

training suitable clinical investigators; • delays in identifying, recruiting, and enrolling patients who meet the requirements of our clinical trials; • delays in obtaining required IRB approval at each clinical trial site; • delays in manufacturing, testing, releasing, validating, or importing / exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing; • insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials; • imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, CTA or amendment, or equivalent foreign application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites; • developments on trials conducted by competitors for related technology that raise FDA or foreign regulatory authority concerns about risk to patients of the technology broadly; or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives; • delays caused by patients withdrawing from clinical trials or failing to return for post- treatment follow- up; • difficulty collaborating with patient groups and investigators; • failure by our CROs, other third parties, or us to adhere to clinical trial protocols; • failure to perform in accordance with the FDA’ s or any other regulatory authority’ s good clinical practice requirements (“ GCP ”) requirements or applicable regulatory guidelines in other countries; • occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits; • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; • changes in the standard of care on which a clinical development plan was based, which may require new or additional trials; • the cost of clinical trials of our product candidates being greater than we anticipate; • clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates; • transfer of manufacturing processes to larger- scale facilities operated by a contract CMO or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; • third parties being unwilling or unable to satisfy their contractual obligations to us; and • adverse public perception or regulatory scrutiny of genetic medicine technology may negatively impact the developmental progress or commercial success of products that we develop alone or with collaborators. ~~In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.~~ Patient enrollment, a determinative factor in the timing of clinical trials, is affected by many factors including the severity of and difficulty of diagnosing the disease under investigation, knowledge of the disease in the medical community and availability of effective diagnostic methods, size and distribution of the patient population and process for identifying subjects, access of patients to medical professionals experienced in their disease, our ability to effectively disseminate information about our clinical trials to the patient population and access of patients to such information, eligibility and exclusion criteria for the trial in question, design of the trial protocol, availability, efficacy of, and our ability to compete with approved and standard of care therapies or other clinical trials for the disease or condition under investigation, perceived risks and benefits of the product candidate under trial or testing, availability of genetic testing for potential patients, efforts to facilitate timely enrollment in clinical trials, patient referral practices of physicians, ability to obtain and maintain subject consent, the risk that enrolled subjects will drop out before completion of the trial, the ability to monitor patients adequately during and after treatment, the time and financial commitments required of patients to enroll in our trials beyond the costs covered by the company, and the proximity and availability of and access to clinical trial sites for prospective patients. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance. Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required, or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may seriously harm our business. We could also encounter delays if a clinical trial is suspended or terminated by us, by the 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. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates and could seriously harm our business. The limited number of patients who have the diseases for which many of our product candidates are being studied may make it more difficult for us to enroll or complete clinical trials or may result in findings in our clinical trials that do not reach levels of statistical significance sufficient for marketing approval. Many of the conditions for which we plan to evaluate our current product candidates in clinical trials are rare genetic diseases. Accordingly, there are limited patient pools from which to draw for clinical trials. In addition to the rarity of these diseases, the eligibility criteria of our clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their disease is either severe enough or not too advanced to include them in

a trial. We or our collaborators may not be able to initiate or continue clinical trials on a timely basis or at all for any of our product candidates if we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Similarly, because many of the conditions we intend to treat are rare in nature, we plan to design and conduct clinical trials utilizing a small number of patients in order to evaluate the safety and therapeutic activity of our product candidates. Conducting trials in smaller subject populations increases the risk that any safety or efficacy issues observed in only a few patients could prevent such trials from reaching statistical significance or otherwise meeting their specified endpoints, which could require us to conduct additional clinical trials, or delay or prevent our product candidates from receiving regulatory approval, which would seriously harm our business. Research and development of biopharmaceutical products is inherently risky. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized or if they will ever be successfully commercialized. We are at an early stage of development of our product candidates. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following: • our product candidates may not successfully complete preclinical studies or clinical trials; • **delays in our clinical development plans due to the COVID-19 pandemic**; • a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it does not meet applicable regulatory criteria; • our competitors may develop therapeutics that render our product candidates obsolete or less attractive; • our competitors may develop platform technologies that render our Therapeutic Vector Evolution platform technology obsolete or less attractive; • the product candidates and Therapeutic Vector Evolution platform technology that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights or may be covered by third- party patents or other intellectual property or exclusive rights; • the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive; • a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; • if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate; • **delays in our clinical development plans due to public health emergencies, such as the COVID- 19 pandemic**; and • a product candidate may not be accepted as safe and effective by patients, the medical community or third- party payors. If any of these events occur, we or our collaborators may be forced to abandon our development efforts for a product candidate or candidates, which would seriously harm our business. Failure of a product candidate may occur at any stage of preclinical or clinical development, and, because our product candidates and our Therapeutic Vector Evolution platform technology are in an early stage of development, there is a relatively higher risk of failure, and we may never succeed in developing marketable products or generating product revenue. We may not be successful in our efforts to further develop our Therapeutic Vector Evolution platform technology and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all. Any clinical trials that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future clinical trials are inconclusive with respect to the efficacy of our product candidates or if we do not meet the clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for our product candidates. If any of our product candidates successfully completes clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would seriously harm our business. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, purity, potency, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing and distribution of our product candidates. We may also rely on our collaborators or collaboration partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or collaboration partners will conduct these activities successfully or do so within the timeframe we desire. Even if we (or our collaborators or collaboration partners) are successful in obtaining approval in one jurisdiction, we cannot **ensure- assure you** that we will obtain approval in any other jurisdictions. Failure to obtain approval for our product candidates in multiple jurisdictions will seriously harm our business. Even if we receive regulatory approval to market any of our product candidates, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Any approval we may obtain could be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a REMS. The failure to obtain timely regulatory approval of product candidates, any product marketing limitations or a product withdrawal would seriously harm our business. Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We

cannot provide any assurance--- **assure you** that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates. Public health crises such as pandemics or similar outbreaks have affected and could continue to seriously and adversely affect our preclinical and clinical trials, business, financial condition and results of operations. **Public health crises, such as** ~~In response to the COVID-19 pandemic~~ **pandemics or similar outbreaks**, “shelter ~~could result~~ **in place**” orders and other public health guidance measures were implemented, and may be implemented again to the extent eased, across much of the United States and Europe, including in the locations of our offices, clinical trial sites, key vendors and partners. We expect that our clinical development program timelines ~~will could~~ **will be negatively affected by such pandemics, any public health orders or measures implemented in response to such pandemics, or residual effects thereof, which could seriously harm our business. Further, in response to COVID-19, which could seriously harm our business. Further, in response to COVID-19 health guidance measures and ~~concerns~~, we have implemented a work- from- home policy for all staff members excluding those working in certain laboratory and manufacturing functions and those necessary to maintain minimum basic operations. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay or otherwise seriously harm our business. For example, with our personnel working from home, some of our research activities that require our personnel **to be in our laboratories will be delayed**. 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 seriously harm our business. The ability of the FDA to review and / or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA’s ability to hire and retain key personnel and accept 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 and biologics to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Separately, in response to the COVID- 19, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations ~~of domestic facilities where feasible~~, ~~the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and~~ any resurgence of the virus or emergence of new variants may lead to ~~further inspectional~~ **or administrative** delays. ~~Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic~~. If a prolonged government shutdown occurs, or if global health concerns ~~continue to~~ 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 seriously harm our business. Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization**, which could seriously harm our business. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we or our collaborators must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Further, because our product candidates are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early- stage or later-stage clinical trials, and results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our ongoing and planned clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could seriously harm our business. In addition, even if such clinical trials are successfully completed, we cannot ~~guarantee~~ **assure you** that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant **additional** resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates,**

the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential. Interim, “top-line” and preliminary data from studies or trials that we announce or publish from time to time may change as more 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 publicly disclose top-line or preliminary data from preclinical studies and clinical trials, which are 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. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line 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. Preliminary or “top-line” 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, top-line and preliminary data should be viewed with caution until the final data are available. From time to time, we 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. Adverse differences between preliminary, top-line or interim data and final data could seriously harm our business. 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 **we determine to be material** information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the top-line **or interim** data that we report differ from final results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could seriously harm our business. We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited, **which could seriously harm our business**. One of our strategies is to identify and pursue preclinical and clinical development and commercialization of additional product candidates through our Therapeutic Vector Evolution platform technology. Our Therapeutic Vector Evolution platform technology may not produce a pipeline of viable product candidates, or our competitors may develop platform technologies that render our Therapeutic Vector Evolution platform technology obsolete or less attractive. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make them unmarketable or unlikely to receive marketing approval. Identifying, developing and obtaining regulatory approval and commercializing additional product candidates will require substantial funding and is prone to the risks of failure inherent in drug development. If we are unable to successfully identify, acquire, develop and commercialize additional product candidates, our commercial opportunity may be limited, **which could seriously harm our business**. We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies and biotechnology companies worldwide. 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. There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of the indications for which we have product candidates, including **XLRP, choroideremia, Fabry disease, wet AMD, and DME, GA, cystic fibrosis lung disease, Fabry disease, X-linked retinitis pigmentosa ("XLRP"), and choroideremia**. Certain of our competitors have commercially approved products for the treatment of the diseases that we are pursuing or may pursue in the future, including **Biogen-Regeneron**, Roche, Sanofi, Takeda and Vertex. These drugs are well established therapies and are widely accepted by physicians, patients and third-party payors, which may make it difficult to convince these parties to switch to our product candidates. Companies that we are aware are developing therapeutics in the ophthalmology, cardiology and pulmonology disease areas include large companies with significant financial resources, such as Allergan, **Biogen-Astellas**, Novartis, Pfizer, **Regeneron**, Roche, Sanofi, Takeda and Vertex, and biopharmaceutical companies such as Adverum, Amicus, **Apellis**, Kodiak Sciences, Krystal, REGENXBIO, Sangamo, and Spirovant. In addition to competition from other companies targeting ophthalmology, pulmonology, and cardiology any products we may develop may also face competition from other types of therapies, such as gene-editing therapies and drug delivery devices. Many of our current or potential competitors, either alone or with their strategic partners, 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. 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 or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our product candidates. 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 any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of ophthalmology, cardiology and pulmonology indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing against competitors any product candidates we may develop. If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they 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 approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing and commercial support infrastructure to sell, or participate in sales activities with our collaborators for some of our product candidates if and when they are approved. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists 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 and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel. Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, compliance, customer service, medical affairs and other support personnel;
- our inability to recruit and build a commercial infrastructure ~~due to the impacts of COVID-19~~;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved 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 commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may 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 commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved and our business would be seriously harmed. Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success. The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- sufficient third-party coverage or reimbursement;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, EMA or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable and our business could be seriously harmed.

Risks Related to Manufacturing We currently **manufacture and test clinical trial material for all of our products internally at our cGMP facility, and we have a development, standing relationships with several contract manufacturing organizations and testing agreement and cooperation agreement with Catalent to manufacture supplies of our product candidates in the future.** Our product candidates require processing steps that are more complex than those required for most chemical and protein pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in

lot failures, product recalls, product liability claims or insufficient inventory, which could delay or prevent the initiation of clinical trials or receipt of regulatory approvals. We may encounter problems achieving adequate quantities and quality of clinical- grade materials that meet FDA, or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. In addition, FDA and other comparable foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other comparable foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches which could be costly to us and otherwise seriously harm our business. We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing process which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies, which could limit our access to additional attractive development programs. Problems in ~~third-party~~ manufacturing processes or facilities also could restrict our ability to meet market demand for our products. Additionally, should our ~~agreement with Catalent~~ **supply needs exceed our internal capabilities and supply** agreements with other parties with whom we have manufacturing agreements be terminated for any reason, there are a limited number of manufacturers who would be suitable replacements, and it would take a significant amount of time to transition the manufacturing to a **replacement alternative manufacturing organization**. Delays in obtaining regulatory approval of our manufacturing process or disruptions in our manufacturing process may delay or disrupt our commercialization efforts. Before we can begin to commercially manufacture our product candidates in third- party or our own facilities, we must obtain regulatory approval from the FDA to market our product using the manufacturing process and facility we proposed in our marketing application. In addition, we must **pass successfully complete** a pre- approval inspection of our manufacturing facility by the FDA before any of our product candidates can obtain marketing approval, if ever. In order to obtain approval of a BLA for our product candidates, we will need to ensure that all of our manufacturing processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop. Delays in developing our manufacturing capabilities or failure to achieve operating efficiencies from it may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines. We have recently completed the build out of approximately 17, 000 square feet of laboratory and manufacturing space at our headquarters in Emeryville, California, a large portion of which we plan to devote to manufacturing activities for our clinical trials under cGMP. We may face delays in the production of clinical supply at our manufacturing facility and cannot guarantee when our facility will be able to produce sufficient quantities of product candidates needed to support our planned clinical trials. Any delays in developing our internal manufacturing capabilities ~~, including any delays due to the COVID-19 pandemic,~~ may disrupt or delay the supply of our product candidates if we have not maintained a sufficient back- up supply of such product candidates through third- party manufacturers. Moreover, changing manufacturing facilities during the clinical development process may also require that we or our collaborators conduct additional studies, make notifications to regulatory authorities, make additional filings to regulatory authorities, and obtain regulatory authority approval for the new facilities, which may be delayed or which we may never receive. We will further need to comply with the FDA' s and applicable foreign regulatory authorities' cGMP requirements for the production of product candidates for clinical trials and, if approved, commercial supply, and will be subject to FDA and comparable foreign regulatory authority inspection. These requirements include the qualification and validation of our manufacturing equipment and processes. We may not be able to develop or acquire the internal expertise and resources necessary for compliance with these requirements. In order to develop internal manufacturing expertise, we may be forced to devote greater resources and management time than anticipated, particularly in areas relating to operations, quality, regulatory, facilities and information technology. We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing processes. If we experience unanticipated employee shortage or turnover in any of these areas, we may not be able to effectively manage our ongoing manufacturing operations and we may not achieve the operating efficiencies that we anticipate from developing these capabilities, which may negatively affect our product development timeline or result in difficulties in maintaining compliance with applicable regulatory requirements. Any such problems could result in the delay, prevention or impairment of clinical development and commercialization of our product candidates and would seriously harm our business. We currently rely and expect to continue to rely on third parties to conduct product manufacturing for certain of our product candidates, and these third parties may not perform satisfactorily. Although we are in process of expanding internal manufacturing capabilities, we currently rely, and expect to continue to rely, on third parties for the production of some of our ~~preclinical study and~~ **planned clinical trial and commercial** materials and, therefore, we can control only certain aspects of their activities. The facilities used by us and our contract manufacturers to manufacture certain of our product candidates must be reviewed by the FDA pursuant to inspections that will be conducted after we submit ~~our a~~ **a** BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP for manufacture of our products.

If we or our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to obtain and / or maintain regulatory approval for our products as manufactured at their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a 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. In addition, we rely on additional third parties to manufacture plasmids used in the manufacture of our product candidates and to perform quality testing, and reliance on these third parties entails risks to which we would not be subject if we manufactured the plasmids ourselves, including: • reduced control for certain aspects of manufacturing activities; • termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us; and • disruptions to the operations of our third- party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider. Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future product candidates. Some of these events could be the basis for FDA or European Union Member State regulatory authority action, including injunction, recall, seizure or total or partial suspension of product manufacture. Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our research studies, preclinical, and clinical development or marketing schedules. Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials required in our manufacturing process, such as plasmids, are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could seriously harm our business. We depend on third- party suppliers for key raw materials used in our manufacturing processes, and the loss of these third- party suppliers or their inability to supply us with adequate raw materials could seriously harm our business. We rely on third- party suppliers for the raw materials required for the production of our product candidates. Our dependence on these third- party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited, and we are likely to get lower priority than our competitors who are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any interruption in supply of raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supplier in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would seriously harm our business.

Risks Related to Regulatory Approval and Other Legal Compliance Matters The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, expensive, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be seriously harmed. We and any collaborators are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. We have not submitted for or obtained regulatory approval for any product candidate. We and any collaborators must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following: • the FDA or comparable foreign regulatory authorities may disagree with the design, implementation or results of our or our collaborators' clinical trials; • the FDA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use of our products; • the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval; • we or our collaborators may be unable to demonstrate to the FDA, or comparable foreign regulatory authorities that a product candidate's clinical and other benefits outweigh its safety risks; • the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere; • the FDA or

comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval. This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would seriously harm our business. In addition, even if we or our collaborators were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a REMS. Regulatory authorities **or other authorities responsible for pricing negotiations** may not approve the price we or our collaborators intend to charge for products we may develop, may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could seriously harm our business. We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval. We may in the future seek an accelerated approval for one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor' s agreement to conduct, in a diligent manner, † confirmatory studies to verify and describe the drug' s clinical benefit. If such confirmatory studies fail to confirm the drug' s clinical benefit, or if the sponsor fails to conduct required confirmatory studies in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. **In addition, in December 2022, President Biden signed an omnibus appropriations bill to fund the U. S. government through fiscal year 2023. Included in the omnibus bill is the Food and Drug Omnibus Reform Act of 2022, which among other things, provided FDA new statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval. Under these provisions, the FDA may require a sponsor of a product seeking accelerated approval to have a confirmatory trial underway prior to such approval being granted.** Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA 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 a BLA for accelerated approval or any other form of expedited development, review or approval. Furthermore, if we decide to submit an application for accelerated approval for any of our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval 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, review or approval 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. Even if we or our collaborators obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny. If one of our product candidates is approved, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing studies, and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs and biologics are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product' s approved label. As such, we may not promote our products " off- label " for indications or uses for which they do not have approval, though we may share truthful and not misleading information that is otherwise consistent with our product' s approved labeling. The holder of an approved application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post- marketing clinical studies to verify the safety and efficacy of our products in general or in

specific patient subsets. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval or label restrictions. If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things: • issue warning letters; • impose civil or criminal penalties; • suspend or withdraw regulatory approval; • suspend any of our clinical trials; • refuse to approve pending applications or supplements to approved applications submitted by us; • impose restrictions on our operations, including closing our manufacturing facility or our contract manufacturers' facilities; or • seize or detain products, or require a product recall. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, our business will be seriously harmed. Moreover, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. 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 be subject to enforcement action and we may not achieve or sustain profitability. We have received Fast Track designation for 4D- 310 for the treatment of Fabry disease, and for 4D- 125 for the treatment of patients with inherited retinal dystrophies due to defects in the RPGR gene, including XLRP, and we may seek Fast Track designation for certain future product candidates. However, we may not be able to obtain such designations, and there is no guarantee that 4D- 310 or 4D- 125 will experience a faster regulatory review or obtain regulatory approval. If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this disease condition, the product sponsor may apply for Fast Track designation. The sponsor of a Fast Track product **candidate** has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the **application product candidate** may be eligible for priority review. A **BLA for a fast-Fast track-Track product candidate** may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. 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. We have received Fast Track designation for 4D- 310 for the treatment of Fabry disease, and for 4D- 125 for the treatment of patients with inherited retinal dystrophies due to defects in the RPGR gene, including XLRP and we may receive Fast Track designation for other product candidates in the future; however, we may not experience a faster development, review or approval process, and receipt of the designation does not increase the likelihood that the FDA will approve 4D- 310 or 4D- 125 for any indication. In addition, the FDA may rescind the Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. We have received orphan drug designation for 4D- **710 for cystic fibrosis, 4D-** 110 for the treatment of choroideremia as well as 4D- 125 for the treatment of patients with inherited retinal dystrophies due to defects in the RPGR gene, including XLRP, and for 4D- 310 for the treatment of Fabry disease, and we may seek orphan drug designation for certain future product candidates. However, we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our revenue, if any, to be reduced. We have received orphan drug designation in the United States for **4D- 710 for the treatment of cystic fibrosis, 4D-** 110 for the treatment of choroideremia and for 4D- 310 for the treatment of Fabry disease. In the European Union, we have received orphan drug designation for 4D- 125 for the treatment of patients with inherited retinal dystrophies due to defects in the RPGR gene, including XLRP, **and for 4D- 310 for the treatment of Fabry disease**. Although we may seek orphan product designation for some or all of our other product candidates, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a drug or biologic product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200, 000 in the United States, or a patient population greater than 200, 000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation must be requested before submitting a BLA. In the European Union, the EMA's Committee for Orphan Medicinal Products ("COMP"), grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10, 000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and 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 receives the first FDA approval for the disease or condition for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same disease or condition for a period of seven years, except in limited

circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity for the orphan patient population. Exclusive marketing rights in the United States may also be unavailable if we or our collaborators seek approval for a disease or condition broader than the orphan designated disease or condition and may be lost if the FDA later determines that the request for designation was materially defective. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. 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. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with for the same condition if the FDA concludes that the later drug is clinically superior in that it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug or biologic nor gives the drug or biologic any advantage in the regulatory review or approval process. **We have received Regenerative Medicine Advanced Therapy ("RMAT") and PRIME designation for 4D- 150 for the treatment of wet AMD. We may seek RMAT and PRIME designations for certain future product candidates, however we may not be able to obtain such designations, and there is no guarantee that 4D- 150 will experience a faster regulatory review or obtain regulatory approval. The FDA has granted RMAT designation for 4D- 150 for the treatment of neovascular (wet) age- related macular degeneration, and may seek additional RMAT designations for 4D- 150 or for our other product candidates. An biological product candidate is eligible for RMAT designation if: (1) it meets the definition of a regenerative medicine therapy, which the FDA defines as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) the candidate is intended to treat, modify, reverse, or cure a serious disease or condition; and (3) preliminary clinical evidence indicates that the candidate has the potential to address unmet medical needs for such disease or condition. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review of BLAs. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long- term clinical benefit, or through reliance upon data obtained from a meaningful number of sites, including through expansion of clinical trials to a sufficient number sites, as appropriate. RMAT- designated product candidates that receive accelerated approval may, as appropriate, be able to fulfill their post- approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real- world evidence (such as electronic health records), through the collection of larger confirmatory data sets, or via post- approval monitoring of patients treated with the therapy prior to approval. RMAT designation is within the sole discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for RMAT designation, the FDA may disagree and instead determine not to make such designation. RMAT designation does not change the standards for product approval, and there is no assurance that such designation or eligibility for such designation will result in expedited review or approval, or that the approved indication will not be narrower than the indication covered by the RMAT designation. PRIME designation is granted by the EMA to enhance support for the development of medicines that target an unmet medical need and offers the opportunity to accelerate review of the marketing applications to bring such medicines to patients sooner. Receipt of these designations does not increase the likelihood that FDA or EMA will approve 4D- 150 for any indication. In addition, the FDA or EMA may rescind the designations if such regulatory agencies believe that the designation is no longer supported by data from our clinical development program. We have obtained a rare pediatric disease designation for 4D- 710, however, there is no guarantee that FDA approval of will result in issuance of a priority review voucher. In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U. S. within one year following the date of approval. We have obtained a rare pediatric disease designation for 4D- 710 for the treatment of cystic fibrosis, however, there is no guarantee that we will be able to obtain a priority review voucher, even if 4D- 710 is approved by the FDA for this indication. For example, the FDA may determine that a BLA, even if ultimately approved, does not meet the eligibility criteria for a priority review voucher, including for the following reasons: • the product no longer meets the definition of a rare pediatric disease; • the product contains an active ingredient (including any ester or salt of the active ingredient) that has been previously approved in another marketing application; • the application does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population; • the application is approved for a different adult indication than the rare pediatric disease for which the product is designated. Moreover, Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Under the current statutory sunset provisions, after September 30, 2024, FDA**

may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the product candidate, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any rare pediatric disease priority review vouchers, regardless of any rare pediatric disease designation.

If the product candidates that we or our collaborators may develop receive regulatory approval in the United States or another jurisdiction, they may never receive approval in other jurisdictions, which would limit market opportunities for such product candidates and seriously harm our business. Approval of a product candidate in the United States by the FDA or by the requisite regulatory agencies in any other jurisdiction does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions. The approval process varies among countries and may limit our or our collaborators' ability to develop, manufacture, promote and sell product candidates internationally. Failure to obtain marketing approval in international jurisdictions would prevent the product candidates from being marketed outside of the jurisdictions in which regulatory approvals have been received. In order to market and sell product candidates in the European Union and many other jurisdictions, we and our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional preclinical studies or clinical trials both before and after approval. In many countries, any product candidate for human use must be approved for reimbursement before it can be approved for sale in that country. In some cases, the intended price for such product is also subject to approval. Further, while regulatory approval of a product candidate in one country does not ensure approval in any other country, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we or our collaborators fail to comply with the regulatory requirements in international markets or to obtain all required marketing approvals, the target market for a particular potential product will be reduced, which would limit our ability to realize the full market potential for the product and seriously harm our business. Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and to commercialize our product candidates and may affect the prices we may set. In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively the "ACA") was enacted, which substantially changed the way healthcare is financed by both governmental and private payors. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following: • an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs; • new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members; • an increase to the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and an extension the rebate program to individuals enrolled in Medicaid managed care organizations; • a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; • expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability; • a licensure framework for follow-on biologic products; • a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and • establishment of a Center for Medicare & Medicaid Innovation ("CMMI") at the Centers for Medicare & Medicaid Services ("CMS") to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial, U. S. Congressional and executive branch challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. ~~Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures, if any, will impact our business.~~In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. ~~These new laws~~ **Additionally, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law** or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers ~~eliminated the statutory Medicaid drug rebate cap for single source and accordingly innovator multiple source drugs~~, seriously harm our business **beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price**. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been

heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U. S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient assistance programs. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). **On August 29, 2023, CMS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges.** We also expect that additional U. S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U. S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures and could seriously harm our business. Individual states in the United States have also increasingly passed legislation and implemented 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. Legally mandated price controls on payment amounts by third- party payors or other restrictions could seriously harm our business. 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. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing. Furthermore, there has been increased interest by third- party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. Prescription drugs and biological products that are in violation of these requirements will be included on a public list. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing and could seriously harm our business. In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or judicial action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. Even if we are able to commercialize any product candidates, due to unfavorable pricing regulations and / or third- party coverage and reimbursement policies, we may not be able to offer such products at competitive prices which would seriously harm our business. The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval. Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and other third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and other third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs (“VA”) hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, other 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. For genetic medicine and other 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. We cannot be sure that reimbursement will

be available for any product candidate that we commercialize and, if reimbursement is available, that the level of reimbursement will be sufficient. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could seriously harm our business. Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time-consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed. We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell any products effectively, if approved, or generate product revenue. We currently do not have a marketing or sales organization. In order to commercialize any product, if approved, in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In advance of any of our product candidates receiving regulatory approval, we expect to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize each such product candidate, which will be expensive and time-consuming. We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates. If we are not successful in commercializing products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses and our business would be seriously harmed. Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties and seriously harm our business. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U. S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be

made, in whole or in part, under any U. S. federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. federal civil and criminal false claims and civil monetary penalties laws, including the civil federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the U. S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U. S. federal government. Pharmaceutical manufacturers can cause false claims to be presented to the U. S. federal government by engaging in impermissible marketing practices, such as the off- label promotion of a product for an indication for which it has not received FDA approval. In addition, the government may assert that a claim including items and services resulting from a violation of the U. S. federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act; • the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U. S. federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation; • the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices; • the U. S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product; • the U. S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to report annually to CMS information related to certain payments and other transfers of value to physicians (as defined by statute), certain other non- physician practitioners (including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants, and certified nurse midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; • analogous U. S. state laws and regulations, including: state anti- kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third- party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U. S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives; and • similar healthcare laws in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers. We may also be subject to additional federal laws, such as the U. S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U. S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof, and federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including certain of our advisory board arrangements with physicians, some of whom are compensated in the form of stock or stock options, 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 civil, criminal and administrative penalties, damages, fines, exclusion from government- funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non- compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. 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 imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time- consuming and may require significant 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. We use and generate materials that may expose us to material liability. Our research programs involve the use of hazardous materials and chemicals. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products such as human tissue samples that may have the potential to transmit diseases. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers’ compensation,

property and business interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims. Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our products. The Animal Welfare Act (“AWA”) is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected. Risks Related to Our Reliance on Third Parties We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing. We currently rely and expect to continue to rely on third parties, such as CROs, CMOs, clinical data management organizations, clinical data assessments and analysis organizations, medical institutions and clinical investigators, to conduct some aspects of our manufacturing, research, preclinical testing and clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities reduces our control over these activities, but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We are also required to register ongoing clinical trials and to post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines. We also expect to rely on other third parties to manufacture, store and distribute drug supplies for our clinical trials. Any performance failure on the part of our manufacturers or distributors could delay clinical development or, marketing approval or commercialization of any product candidates we may develop or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue. We rely on various CROs to obtain NHPs for use in vector discovery and preclinical development work. In February 2023, we were informed that Charles River Laboratories (“Charles River”), one of our primary suppliers of NHPs, received a subpoena from the United States Department of Justice with respect to its importation of NHPs from Cambodia. Charles River reported that it has voluntarily suspended NHP shipments from Cambodia at this time. If we are unable to secure adequate supply of NHPs from Charles River or other CROs, or the shortage of NHPs causes the price of NHPs to rise substantially, certain of our vector discovery projects and preclinical development efforts will be delayed, and the cost of conducting discovery projects and preclinical development activities may substantially increase. Such delays or cost increases could materially adversely affect our discovery and preclinical development activities and our business. We may depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates. We have sought, and may in the future seek, third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional, national and international pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities 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 product candidates we may develop, pose the following risks to us: • collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations; • collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property; • collaborators may own or co-own intellectual property covering our product candidates that result from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates; • disputes may arise with respect to the ownership of intellectual property developed pursuant to collaborations; • we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us; • collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; • 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; • collaborators may decide not to pursue development

and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our 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 with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates; • we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control; • collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction which is not in our best interest; • collaborators may become party to a business combination transaction and the continued pursuit and emphasis on our development or commercialization program by the resulting entity under our existing collaboration could be delayed, diminished or terminated; • collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, devices, materials, know-how or intellectual property of the collaborator relating to our products and product candidates; • key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators; • collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business; • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or our Therapeutic Vector Evolution platform technology; and • collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and 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 or delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue which could seriously harm our business. If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also 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. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section, and any negative impact on our collaborators may adversely affect us. Risks Related to Our Intellectual Property Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. Further, we have ~~one three~~ **one three** granted ~~patent patents~~ (U. S. patent ~~no nos~~ **nos. 11, 136, 557, 11, 634, 691 and 10, 988, 519**) and ~~three four~~ **three four** pending patent applications (U. S. patent application nos. 16 / 486, 681, 17 **, 468, 290, 17 725-156, 289-023 and 17-18 / 184, 184 468, 290**), that were made with government support, that may be subject, under certain circumstances, to march-in rights under 35 U. S. C. 203, which is a right that allows the government, in certain limited circumstances, to force a party with a license to intellectual property funded, at least in part, by the government, to grant a license to such property to another entity. U. S. patent **nos. 11, 136, 557 and 11, 634, 691 were made with the support of U. C. Berkeley and relate to our A101 vector of our 4D- 710 and 4D- 725 product candidates. U. S. patent no. 11-10, 136-988, 557-519** was made with the support of **University of Pennsylvania U-C: Berkeley** and relates to our **A101 vector short- form human complement factor H (sCFH) payload of our 4D- 175 product candidate**. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our product candidates and proprietary technologies and erode or negate any competitive advantage we may have, which could seriously harm our business. We and

our licensors have applied, and we intend to continue applying, for patents covering aspects of our product candidates, proprietary technologies and their uses that we deem appropriate. However, we may not be able to apply for patents on certain aspects of our current or future product candidates, proprietary technologies and their uses in a timely fashion, at a reasonable cost, in all jurisdictions, or at all, and any potential patent coverage we obtain may not be sufficient to prevent substantial competition. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators or licensors will be successful in protecting our product candidates, proprietary technologies and their uses by obtaining and defending patents. These risks and uncertainties include the following:

- the U. S. Patent and Trademark Office (“USPTO”) and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;
- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same methods or devices or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any products or product candidates that we may develop;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates, proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our licensors' patent applications for any patent application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U. S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. 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 patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. Moreover, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents, if issued, patents obtained by our collaborators or the patent rights that we license from others, may be challenged in the courts or patent offices in the United States and abroad. Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. Such challenges 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 or identical products or product candidates, or limit the duration of the patent protection of our product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering our product candidates are invalidated or found unenforceable, or if a court found that valid, enforceable patents held by third parties covered one or more of our product candidates, our competitive position could be harmed or we could be required to incur significant expenses to enforce or defend our rights. If we initiate lawsuits to protect or enforce our patents, or litigate against third-party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel. The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- any of our pending patent applications or those of our licensors may issue as patents;
- others will not or may not be able to make, use, offer to sell, or sell products that are the same as or similar to our own but that are not covered by the claims of the patents that

we own or license; • we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire; • we or our licensors were the first to make the inventions covered by each of the patents and pending patent applications that we own or license; • we or our licensors were the first to file patent applications for these inventions; • others will not develop similar or alternative technologies that do not infringe the patents we own or license; • any of the patents we own or license will be found to ultimately be valid and enforceable; • any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable products or will provide us with any competitive advantages; • a third party may not challenge the patents we own or license and, if challenged, a court would hold that such patents are valid, enforceable and infringed; • we may develop or in- license additional proprietary technologies that are patentable; • the patents of others will not have an adverse effect on our business; • our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we will develop additional proprietary technologies or product candidates that are separately patentable; or • our commercial activities or products will not infringe upon the patents of others. Where we obtain licenses from or collaborate with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could seriously harm our business. Furthermore, our owned and in- licensed intellectual property rights may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our in- licensed patent rights and technology was funded in part by the U. S. government. As a result, the government may have certain rights, or march- in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non- exclusive license authorizing the government to use the invention for non- commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march- in rights to use or allow third parties to use our licensed technology. The government can exercise its march- in rights if it determines that action is necessary because we fail to achieve practical application of the government- funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U. S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could seriously harm our business. The lives of our patents may not be sufficient to effectively protect our product candidates and business. Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective non- provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, are limited. Even if patents covering our product candidates, proprietary technologies and their uses are obtained, once the patent life has expired, we may be open to competition. In addition, although upon issuance in the United States a patent' s life can be extended based on certain delays caused by the USPTO and clinical development, this extension can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. If we do not have sufficient patent life to protect our product candidates, proprietary technologies and their uses, our business would be seriously harmed. If we are unable to protect the confidentiality of our trade secrets, our business would be seriously harmed. We rely on the protection of our trade secrets, including unpatented know- how, technology and other proprietary information to maintain our competitive position. We have taken steps to protect our trade secrets and unpatented know- how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees and consultants. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant or third party with authorized access. Our security measures may not prevent an employee, consultant, collaborator or third party from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. 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. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our product candidates that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time- consuming, and the outcome is unpredictable. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our employees, collaborators, licensors, third- party contractors

and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we have relied on, and in future expect to rely on third parties in the development, manufacture, and distribution of our product candidates and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized. We currently are reliant upon licenses of certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology, including technology related to our product candidates. For example, we rely on our exclusive license agreements with **i) U. C. Berkeley for certain rights with respect to the intellectual property covering certain compositions of matter and methods of use of certain AAV variants related to our 4D- 710 and 4D- 725 product candidates**, **and ii) University of Pennsylvania for certain rights with respect to the intellectual property covering certain compositions of matter and methods of use of the short- form human complement factor H (sCFH) payload related to our 4D- 175 product candidate**. These and other licenses we may enter into in the future may not provide adequate rights to use such intellectual property and technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize our technology and product candidates in the future. As a result, we may not be able to develop and commercialize our technology and product candidates in fields of use and territories for which we are not granted rights pursuant to such licenses. Licenses to additional third- party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could seriously harm our business. In some circumstances, we may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know- how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our product candidates. We also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in- license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products. Our current licenses, and our future licenses likely will, impose various royalty payments, milestones, and other obligations on us. If we fail to comply with any of these obligations, we may be required to pay damages and the licensor may have the right to terminate the license. Termination by the licensor would cause us to lose valuable rights, and could prevent us from developing and commercializing our product candidates and proprietary technologies. Our business would be seriously harmed if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor' s rights. In addition, while we cannot currently determine the amount of royalty obligations we would be required to pay on the sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in product candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize any product candidates, we may be unable to achieve or maintain profitability. If our trademarks and trade names, whether registered in the future or unregistered now, 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. Any trademarks we may register in the future or any current unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors 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 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. We may license our trademarks and trade names, to the extent any are registered, to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to

enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could seriously harm our business. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make genetic medicine products that are similar to our product candidates or utilize similar genetic medicine technology but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could seriously harm our business. Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products. Any future collaborations that we enter into may not be successful, such as our collaboration agreement with Pfizer that was terminated in 2018, with AstraZeneca that concluded in 2020 without AstraZeneca exercising its option and with Roche that was terminated without cause effective September 2021. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to 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 trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators could independently develop, or develop with third parties, products and product candidates that compete directly or indirectly with our product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products and product candidates may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future product candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may adversely affect the price of our common stock and may result in a need for additional capital to pursue further development or commercialization of the applicable current or future product candidates;
- collaborators may own or co-own intellectual property covering our product candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Related to Our Operations We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate and retain highly qualified managerial, scientific and medical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business. We conduct our operations at our facilities in Emeryville, California, in a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region, and doing so may be costly and difficult. To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock option grants. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. In addition, our employees are employed at-will, which means that any of our employees could leave our employment at any time, with or without notice. If we are unable to attract, incentivize and retain quality personnel on acceptable terms, or at all, it could seriously harm our business. We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth. As of December 31, 2022-2023, we had 140-147 full-time employees. As our development plans and strategies develop, we must add a significant number of additional managerial, operational, financial and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;
- expanding our operational, financial and management controls, reporting systems and procedures; and
- managing increasing operational and managerial

complexity. Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities. We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development and commercialization goals. Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the U. S. dollar would make those clinical trials more costly to operate. Furthermore, a severe or prolonged economic downturn, including a recession or depression resulting from the **current lingering effects of the COVID-19 pandemic** or other factors such as increased inflation or closure of or liquidity issues at financial institutions (including, for example, Silicon Valley Bank) could result in a variety of risks to our business, including weakened demand for our product candidates or any future product candidates, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption, including any international trade disputes, could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our potential products. Any of the foregoing could seriously harm our business, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could seriously harm our business. If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks. We may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any acquisition or strategic partnership may entail numerous risks, including: • increased operating expenses and cash requirements; • the assumption of indebtedness or contingent liabilities; • the issuance of our equity securities which would result in dilution to our stockholders; • assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel; • the diversion of our management's attention from our existing product candidates and initiatives in pursuing such an acquisition or strategic partnership; • retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships; • risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and • our inability to generate revenue from acquired intellectual property, technology and / or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs. In addition, if we undertake such a transaction, we may incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Our information technology systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches and other disruptions. We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information of customers and our employees and contractors. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. Despite the implementation of security measures, our internal information technology systems and those of our collaborators, future CROs and other contractors and consultants may be vulnerable to attack, damage and interruption from computer viruses and malware (e. g. ransomware), malicious code, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, denial or degradation of service attacks, **and sophisticated nation-state and nation-state supported actors** ~~unauthorized access or use, persons inside our organization, or persons with access to systems inside our organization~~. The risk of a security breach or disruption, particularly through cyberattacks 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. **We** ~~As a result of the COVID-19 pandemic, we~~ and our third party service providers and partners may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may experience security breaches that may remain undetected for an extended period. 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. Our third party service providers and partners are also subject to these heightened risks. The costs to us to investigate and mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we

have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service, negative publicity and other harm to our business and our competitive position. We and certain of our service providers have experienced certain cyberattacks and security incidents from time to time. Although to our knowledge we have not experienced any significant system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss, corruption or unauthorized disclosure of our trade secrets, personal data or other proprietary or sensitive information or other similar disruptions. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of clinical trial data or personal data, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media, and other parties pursuant to privacy and security laws. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their information technology systems could also seriously harm our business. Any security compromise affecting us, our partners or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures, and lead to regulatory scrutiny. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary or personal information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed. Any losses, costs or liabilities may not be covered by, or may exceed the coverage limits of, any applicable insurance policies. Business disruptions could seriously harm our business. Our operations, and those of our CROs, CMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our business. All of our operations including our corporate headquarters are located in multiple facilities in Emeryville, California. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, earthquake and other natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business could be seriously harmed by such delays and interruption. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the United States and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could seriously harm our business. As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations implemented thereunder (collectively, "HIPAA"), imposes, among other things, certain standards on certain health care providers, health plans, and health care clearinghouses, 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. We may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA. Certain states have also adopted comparable privacy and security laws and regulations, which govern the privacy, processing and protection of health-related and other personal information. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, California enacted the CCPA on June 28, 2018, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that ~~has is expected to increase~~ **increased the likelihood of, and risks associated with** data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. Further, the CPRA ~~generally, which~~ went into effect on January 1, 2023, ~~and~~ significantly amends the CCPA ~~and~~ **It** imposes additional data protection obligations on covered businesses, including additional consumer rights

processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also ~~creates~~ **created** a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may be required. Similar laws have passed in ~~Virginia, Colorado, Utah, and Connecticut, and have been proposed in~~ other states and **are continuing to be proposed** at the ~~state and~~ federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. In Europe, the GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the European Economic Area (“ EEA ”). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant undertaking, whichever is greater. **In addition to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease or change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and / or civil claims (including class actions).** Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EEA and the United States remains uncertain. **Case law from** For example, in July 2020, the **Court of Justice of the European Union (“ CJEU ”)** ~~limited how organizations could lawfully transfer personal data from the EEA to the United States~~ **states that reliance by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on use of the standard contractual clauses (“ SCCs ”) – a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism – alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case- by- case basis**. ~~In March~~ **On October 7, 2022, the US President Biden signed and – an EU announced a Executive Order on ‘ Enhancing Safeguards for United States Intelligence Activities’ which introduced new regulatory regime intended – redress mechanisms and binding safeguards to replace – address the invalidated concerns raised by the CJEU in regulations – – relation ; however, this – to data transfers from the EEA to the United States and which formed the basis of the** new EU- US Data Privacy Framework (“ DPF ”), ~~has – as released not been implemented beyond an executive order signed by President Biden on October 7~~ **December 13, 2022**. **The European Commission adopted its Adequacy Decision in relation to the DPF on Enhancing Safeguards July 10, 2023, rendering the DPF effective as a GDPR transfer mechanism to U. S. entities self- certified under the DPF. The DPF also introduced a new redress mechanism for EU citizens which addresses a key concern in the previous CJEU judgments and may mean transfers under standard contractual clauses are less likely to be challenged in future. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the** ~~United States Signals Intelligence Activities. European court and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulatory – regulators . As a result, we may decisions subsequent to the CJEU decision of July 2020 have taken a restrictive approach to make certain international – operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing~~ **data transfers within required time frames**. As the enforcement landscape further develops, and supervisory authorities issue further guidance on – and revised SCCs for – international data transfers, we could suffer additional costs, complaints and / or regulatory investigations or fines; we may have to stop using certain tools and vendors and make other operational changes; and / or it could otherwise affect the manner in which we provide our services, and could adversely affect our business, operations and financial condition. Further, from January 1, 2021, companies have had to comply with the GDPR and also the United Kingdom GDPR, or the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i. e., fines up to the greater of € 20 million (£ 17. 5 million) or 4 % of global turnover. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. ~~Failure~~ **Additionally, the Securities and Exchange Commission (the “ SEC ”) recently adopted a rule that enhances and standardizes disclosures regarding cybersecurity risk management and governance, as well as material cybersecurity incidents. Under this new rule, we will be required to make annual disclosures describing or our perceived failure processes for identifying and managing material cybersecurity risks, management’ s role in assessing and managing such risks and our board of directors’ oversight of cybersecurity risks. We will also be required to disclose, in a Current Report on Form 8- K, the nature, scope and timing of any material cybersecurity incidents identified and the material impact or reasonably likely material impact on the company. We expect to face increased costs to comply with this new SEC the GDPR, the UK GDPR, and other countries’ privacy or data security – cybersecurity – related laws, rules – rule, including increased costs or for cybersecurity training** regulations could result in significant regulatory penalties and fines, affect our compliance with contracts entered into with our partners, collaborators and other third- party payors, and could have an ~~and management adverse effect on our reputation, business and financial condition~~. Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, CROs, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and seriously harm our business – Our ability to use our net operating loss carryforwards and certain other tax attributes may be

limited. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended (the “ Code ”), if a corporation undergoes an “ ownership change ” (generally defined as a greater than 50- percentage- point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three- year period), the corporation’ s ability to use its pre- change net operating loss carryforwards (“ NOLs ”) and other pre- change tax attributes to offset its post- change taxable income or taxes may be limited. If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre- change NOLs or other pre- change tax attributes if we undergo a future ownership change. We have experienced ownership changes in the past. We may also experience ownership changes as a result of any future shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our NOLs and other pre- change tax attributes to offset post- change taxable income or taxes may be subject to limitation. We will be unable to use our NOLs or other tax attributes if we do not attain profitability sufficient to offset our available NOLs or other tax attributes prior to their expiration, to the extent subject to expiration. Changes in tax laws or regulations that are applied adversely to us or our customers may seriously harm our business. New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of any of our future domestic and foreign earnings. Any new taxes could adversely affect our domestic and international business operations, and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us.

Risks Related to Ownership of Our Common Stock The market price of our common stock may be volatile, which could result in substantial losses for investors. Some of the factors that may cause the market price of our common stock to fluctuate include: • results from, and any delays in, our clinical trials for our clinical- stage product candidates or any other future clinical development programs, including any delays related to the COVID-19 pandemic; • the success of existing or new competitive products or technologies; • commencement or termination of collaborations for our product candidates; • failure or discontinuation of any of our product candidates; • failure to develop our Therapeutic Vector Evolution platform technology; • results of preclinical studies, clinical trials or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors; • regulatory or legal developments in the United States and other countries, including sanctions imposed by either the U. S. or foreign governments; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the commencement of litigation; • the level of expenses related to any of the research programs or product candidates that we may develop; • the results of our efforts to develop additional product candidates or products; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • announcement or expectation of additional financing efforts; • sales of our common stock by us, our insiders, or other stockholders; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in estimates or recommendations by securities analysts, if any, that cover our stock; • changes in the structure of healthcare payment systems; • the impact of political instability, natural disasters, war and / or events of terrorism, such as the war between Ukraine and Russia, and the corresponding tensions created from such conflict between Russia, the United States and countries in Europe as well as other countries such as China; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry, and market conditions; and • the other factors described in this “ Risk Factors ” section. In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Further, the stock market in general has been highly volatile due to the COVID- 19 pandemic, macroeconomic factors such as higher inflation and increased interest rates and political uncertainty in the United States. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Since the completion of our initial public offering in December 2020, the price of our common stock has been volatile, and we expect such volatility to continue. Following periods of such volatility in the market price of a company’ s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management’ s attention and resources from our business. If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We currently have research coverage by seven financial analysts. If one or more of these analysts should drop research coverage of us or if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. Sales of a substantial number of shares of our common stock in the public market could occur at any time, which could cause the market price of our common stock to decline significantly, even if our business is doing well. Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales or the perception in the market that the holders of a large number of shares of our common stock intend to sell shares, could reduce the market price of our common stock. Further, shares issued upon the exercise of stock options outstanding under our equity incentive plans, or pursuant to future awards granted under those plans, will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended (the “ Securities Act ”). Moreover, holders of an aggregate of ~~11~~ **approximately 1.69** million shares of our common stock have rights, subject to 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. Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. We will seek additional capital through one or a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing

arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future offerings. To the extent that we raise additional capital through the sale of equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us. Insiders have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control. Our directors, executive officers, holders of more than 5 % of our outstanding stock and their respective affiliates beneficially own shares representing approximately 55-60% of our outstanding common stock as of December 31, 2022-2023. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock. We are an “ emerging growth company ” and a “ smaller reporting company ” and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors. We are an “ emerging growth company, ” as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, 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. In addition, as an “ emerging growth company ” the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult. We cannot predict if investors will find our common stock less attractive because we will 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. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) December 31, 2025, (2) the last day of the year in which we have total annual gross revenue of at least \$ 1. 07-235 billion, (3) the last day of the year in which we are deemed to be a “ large accelerated filer ” as defined in Rule 12b- 2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded \$ 700. 0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than \$ 1. 0 billion in non- convertible debt securities during the prior three- year period. Even after we no longer qualify as an “ emerging growth company, ” we may still qualify as a “ smaller reporting company, ” which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including, among other things, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act, presenting only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10- K and reduced disclosure obligations. We will incur significant costs as a result of operating as a public company, and our management will devote devotes substantial time to new public company compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes- Oxley Act of 2002, which could result in sanctions or other penalties that would seriously harm our business. We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of the Nasdaq Global Select Market and the rules of the Securities and Exchange Commission (“ SEC ”)-require that we satisfy certain corporate governance requirements relating to director independence, filing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations have and will likely continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms. We are subject to Section 404 of The Sarbanes- Oxley Act of 2002 (“ Section 404 ”) and the related rules of the SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth

companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or, when required to do so, our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. In order to report our results of operations and financial statements on an accurate and timely basis, we will depend in part on CROs to provide timely and accurate notice of their costs to us. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock. Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our Company may deem advantageous. These provisions, among other things:

- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- provide that our directors may be removed only for cause;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- provide for a staggered board, which will result in only a few directors being up for re- election in each calendar year;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws;
- require the affirmative vote of at least 66 2 / 3 % or more of the outstanding shares of our common stock to amend many of the provisions described above; and
- limit the liability of, and provide indemnification to, our directors and officers.

In addition, Section 203 of the General Corporation Law of the State of Delaware (“ DGCL ”) prohibits a publicly- held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15 % of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Any provision of our certificate of incorporation, bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock. Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third- party claims against us and may reduce the amount of money available to us. Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person’ s conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for certain disputes between us and our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation and 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, in the event that the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) **is shall, to** the **fullest extent permitted by law, by the sole and** exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to

enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws will also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act, **including all causes of action asserted against any defendant to such complaint**. Nothing in our amended and restated certificate of incorporation and amended and restated bylaws precludes stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. 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, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could seriously harm our business. **Any person or entity purchasing or otherwise acquiring any interest in our shares of capital stock shall be deemed to have notice of and consented to this exclusive forum provision, but will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.** We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock. We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it. **Unfavorable conditions** ~~The continuation of hostilities in~~ **the global economy caused by global political unrest or conflicts, including the ongoing conflict between Russia and Ukraine and in Israel and Gaza,** may exacerbate certain risks we face. **Political unrest, international conflict, terrorism or war, such as** Russia's invasion of Ukraine **and the armed conflict in February 2022 Israel and Gaza,** and the global response **to these conflicts**, including the imposition of sanctions by the United States and other countries, could create or exacerbate risks facing our business. We have evaluated our operations and partner contracts, and we currently do not expect ~~the existing conflict~~ **conflicts** to directly have a significant effect on our financial condition or results of operations. However, if ~~the~~ hostilities persist, escalate or expand, risks that we have identified in this Quarterly Report on Form 10-Q may be materially increased. For example, if our supply arrangements or clinical operations are disrupted due to expanded sanctions or involvement of countries where we have operations or relationships, our business could be materially disrupted. Further, the use of cyberattacks could expand as part of the ongoing **conflict conflicts**, which could adversely affect our ability to maintain or enhance our cyber security measures. These and other risks are described more fully in this "Risk Factors" section. General Risk Factors Any legal proceedings or claims against us could be costly and time-consuming to defend and could harm our reputation regardless of the outcome. We may in the future become subject to legal proceedings and claims that arise in the ordinary course of business, such as disputes or employment claims made by our current or former employees. Any litigation, whether meritorious or not, could harm our reputation, will increase our costs and may divert management's attention, time and resources, which may in turn seriously harm our business. Insurance might not cover such claims, might not provide sufficient payments to cover all the costs to resolve one or more such claims, and might not continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs and could seriously harm our business. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates. We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to cease commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased or interrupted demand for our products; • substantial monetary awards to trial participants or patients; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • injury to our reputation; • withdrawal of clinical trial participants and inability to continue clinical trials; • initiation of investigations by regulators; • costs to defend the related litigation; • a diversion of management's time and our resources; • loss of revenue; • exhaustion of any available insurance and our capital resources; • the inability to commercialize any product candidate; and • a decline in our share price. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have

various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, research or commercial partners or other collaborators, including the foundations we work with, and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA, EMA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA and other comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could seriously harm our business, including the imposition of significant fines or other sanctions. 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 costs that could seriously harm our business. 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 and biological materials. 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 our current or past facilities and 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, product development and manufacturing 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 biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or 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, which could seriously harm our business. Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. Reliance on third parties to conduct clinical trials, assist in research and development and to manufacture our product candidates, will at times require us to share trade secrets with them. We seek to protect our proprietary technology by in part entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, 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, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may seriously harm our business. We may fail to comply with any of our obligations under existing or future agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business. We are party to various agreements that we depend on to operate our business. Our rights to use currently licensed intellectual property, or intellectual property to be licensed in the future, are or will be subject to the continuation of and our compliance with the terms of these agreements. These agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations which could lead to disputes, including but not limited to those regarding: • the scope of rights granted under the license agreement and other interpretation-related issues; •

the extent to which our proprietary technology and product candidates infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights; • diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the ownership of inventions and know-how resulting from the creation or use of intellectual property by us or our counterparties, alone or jointly; • the scope and duration of our payment obligations; • rights upon termination of such agreement; and • the scope and duration of exclusivity obligations of each party to the agreement. The resolution of any contractual interpretation dispute that may arise, if unfavorable to us, could seriously harm our business. Such resolution could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, increase what we believe to be our financial or other obligations under the relevant agreement, or decrease the third party's financial or other obligations under the relevant agreement. If disputes over intellectual property rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current license agreements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we fail to comply with our obligations under current or future license agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements. Litigation or other proceedings or third-party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our products. Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. We cannot assure you that our operations do not, or will not in the future, infringe existing or future patents or other proprietary rights of third parties. Third parties may have or obtain patents or other proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and future approved products, if any, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexaminations, inter partes review proceedings and post-grant review proceedings before the USPTO and / or corresponding foreign patent offices. Numerous third-party U. S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U. S. patent applications that will not be filed outside the United States can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, 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. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our product candidates. As a result, we may be unaware of third-party patents that may be infringed by commercialization of our product candidates, and cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could: • result in costly litigation; • divert the time and attention of our technical personnel and management; • cause development delays; • prevent us from commercializing our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law; • require us to develop non-infringing technology, which may not be possible on a cost-effective basis; • require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property; • require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing; and / or • require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all. Although no third party has asserted a claim of patent infringement against us as of the date of this

report, others may hold proprietary rights that could prevent our product candidates or any future products from being marketed. Any patent- related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates or proprietary technologies could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates or any future products. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be time-consuming and a substantial diversion of management and employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Even if such licenses are available, we could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins, and the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. In addition, we cannot be certain that we could redesign our product candidates or proprietary technologies to avoid infringement, if necessary, or on a cost- effective basis. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates or any future products which could seriously harm our business. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology. If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. Also, we may be obligated under our agreements with our collaborators, licensors, suppliers and others to indemnify and hold them harmless for damages arising from intellectual property infringement by us. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged. Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. In addition, in a patent infringement proceeding, a court or administrative tribunal may decide that a patent we own or license is not valid, is unenforceable and / or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and / or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non- enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and may result in the revocation, cancellation, or amendment of any foreign patents we hold in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we could lose at least part, and perhaps all, of the patent protection on an affected product candidate. Such a loss of patent protection would seriously harm our business. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO, or equivalent actions brought in foreign jurisdictions, may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be seriously harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non- exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our 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 conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace and seriously harm our business. 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. There could also 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 material adverse effect on the price of our common stock. We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and licenses. We currently have rights to the intellectual property, through licenses from

third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will depend in part on our ability to acquire, license or use these proprietary rights. We may be unable to acquire or license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash 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 have collaborated with a U. S. academic institution and may in the future collaborate with U. S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may 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 other parties, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business could be seriously harmed. We may be subject to claims that we have wrongfully hired an employee from a competitor or that we, our employees or consultants have wrongfully used or disclosed alleged confidential information or trade secrets of their former or concurrent employers or former or current clients. As is common in the biotechnology and biopharmaceutical industries, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. We may also be subject to claims that patents and applications we have filed to protect inventions of our employees or consultants, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer or former or current client. 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, which could seriously harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management and other employees. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. Our agreements with employees and consultants provide that any inventions conceived by an individual in the course of rendering services to us shall be our exclusive property. Although our policy is to have all such individuals complete these agreements, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property may not be self-executing and despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. We may also be subject to claims that former employees, consultants, or other third parties have an ownership interest in our patents or other intellectual property. In addition, we may face claims by third parties that our agreements with employees or consultants obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could seriously harm our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to our management and other employees. If we do not obtain patent term extension for our product candidates, our business may be seriously harmed. Depending upon the timing, duration and specifics of FDA marketing approval of any of our product candidates, one or more of our U. S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch- Waxman Act allows a maximum of one patent to be extended per FDA approved product as compensation for the 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 and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, 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. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration of the applicable product, and our business may be seriously harmed. Changes in patent law in the United States or in other countries could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Our patent rights may be affected by developments or uncertainty in the U. S. or foreign patent statutes, patent case laws, USPTO rules and regulations or in the rules and regulations of foreign patent offices. There are a number of recent changes to the U. S. patent laws that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, the Leahy- Smith America Invents Act (“ Leahy- Smith Act ”) was signed into law. The Leahy- Smith Act includes a number of significant changes to the U. S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy- Smith Act, the United States transitioned in March 2013 to a “ first to file ” system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post- grant proceedings including opposition, derivation, reexamination, inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. This could have a negative impact on some of our intellectual property and could increase uncertainties surrounding obtaining and enforcement or defense of our issued patents. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future. Similarly, statutory or judicial changes to the patent laws of other countries may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending all current and future patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. 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. 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 business may be seriously harmed. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and / or applications. We employ reputable professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patents and patent applications that we own, and if we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. 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. However, there are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. Our business could be negatively impacted by corporate citizenship and ESG matters and / or our reporting of such matters. Institutional, individual, and other investors, proxy advisory services, regulatory authorities, consumers and other stakeholders are increasingly focused on environmental, social and governance (“ ESG ”) practices of companies. As we look to respond to evolving standards for identifying, measuring, and reporting ESG metrics, our efforts may result in a significant increase in costs and may nevertheless not meet investor or other stakeholder expectations and evolving standards or regulatory requirements, which may negatively impact our financial results, our reputation, our ability to attract or retain employees, our attractiveness as an investment or business partner, or expose us to

government enforcement actions, private litigation, and actions by stockholders or stakeholders. 106