Risk Factors Comparison 2025-04-15 to 2024-03-18 Form: 10-K

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You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10- K. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. The risks described below are not the only risks facing us. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, results of operations and prospects. Risks Related to Our Financial Position and Need for Capital

There is substantial doubt regarding our ability to continue as a going concern. We ~~have incurred significant~~ **will need to raise substantial additional funding to finance our** ~~operating~~ **operations through regulatory approval of** ~~losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or~~ **our lead program and beyond** , ~~if achieved,~~ **which may not** be ~~able to sustain profitability~~ **available on acceptable terms, or at all** . ~~We have incurred significant~~ **If we fail to obtain additional capital necessary to fund our** ~~operating~~ **operations ,** ~~losses since~~ we **could be forced** ~~were founded in 2006 and expect~~ to ~~incur significant losses~~ **delay, limit, reduce** ~~for~~ **or terminate** ~~the foreseeable future as we continue development of~~ our product ~~candidates. Losses have resulted principally from costs incurred in our research and~~ development programs ~~and from~~ **, commercialization efforts** ~~our~~ **or** ~~general and administrative expenses. In the future, we intend to continue to conduct research and development, regulatory compliance activities and, if any of our product candidates is approved, sales, marketing and~~ other **operations** ~~activities that~~ , ~~together with anticipated general and administrative expenses, will likely result in us incurring significant losses for~~ **or** ~~the next several years or longer. We currently generate no revenue from sales, and we may never be able~~ to **cease operations** ~~commercialize any of our~~ **or liquidate** ~~product candidates. We do not currently have the required approvals to market any of our product candidates, and we may never receive such approvals. We may not be profitable even if we or~~ **our assets** ~~any development partners succeed in commercializing any of our product candidates~~ . ~~Because~~ **As** of **December 31** ~~the numerous risks and uncertainties associated with developing and commercializing our product candidates~~ , **2024** ~~we are unable to predict the extent of any future losses or when we will become profitable~~ , ~~if at all. We expect that~~ our cash, cash equivalents ~~,~~ and short- term investments ~~will be sufficient~~ **totaled $ 125. 7 million, which we expect** to fund our ~~planned~~ operations into ~~late~~ **the second half of** 2025. ~~If this expectation proves to be wrong, we may be forced to delay, limit or terminate certain of our development efforts before then.~~ We ~~currently expect~~ **have determined that** our **existing** cash ~~,~~ **and** cash equivalents ~~and short~~ **as of December 31, 2024 would be insufficient to fund our operations through one year from the filing date of this Annual Report on Form 10** - ~~term investments~~ **K. Because our cash and cash equivalents will not be adequate** to fund our ~~planned~~ operations ~~into~~ **through at least 12 months from the** ~~late~~ **date** ~~2025. However,~~ **the consolidated financial statements in** this ~~estimate~~ **Annual Report on Form 10- K are issued, there** is ~~based~~ **substantial doubt regarding our ability to continue as a going concern. As a result, the report from our independent registered public accounting firm issued in connection with this Annual Report** on **Form 10- K contains statements expressing substantial doubt** ~~a number of assumptions that may prove to be wrong, including our expectations~~ about ~~the timing of planned clinical trials, investments into~~ our **ability to** ~~manufacturing capabilities, the scope of our research and development activities, continued~~ - **continue as** ~~compliance with and receipt of rental income under our sublease, and changing circumstances beyond our control, that may cause capital to be consumed more rapidly than currently anticipated. As~~ a **going concern** ~~result, our operating plan may change, and we may need to seek additional funds sooner than planned through collaboration agreements and public or private financings. If we run low on capital and are unable to successfully raise additional funds on terms acceptable to us, we may need to significantly curtail some or all of our development activities. We will need to raise additional funding, which may not be available on acceptable terms, or at all. If we fail to obtain additional capital necessary to fund our operations, we will be unable to successfully develop and commercialize our product candidates. We will require substantial future capital in order to complete the nonclinical and clinical development for our product candidates and potentially to commercialize these product candidates~~ . Any future clinical trials or ongoing clinical trials of our product candidates could cause an increase in our spending levels, as ~~would~~ **could** other corporate activities, such as expenses related to manufacturing supply of our product candidates. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including: • the type, number, scope, progress, costs, results of and timing of any future nonclinical studies and clinical trials of any of our product candidates that we are pursuing or may choose to pursue in the future; • the need for, and the progress, costs and results of, any additional clinical trials or nonclinical studies of our product candidates we may initiate based on the results of any clinical trials that we may plan or discussions with the United States Food and Drug Administration ~~(" FDA ")~~ or other regulatory authorities outside the United States ~~(" U. S. ")~~ , including any additional clinical trials or nonclinical studies the FDA or other regulatory authorities outside the U. S. may require evaluating the safety of our product candidates; • the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights; • the costs and timing of obtaining or maintaining manufacturing for our product candidates, including **commercial validation and** internal and external commercial manufacturing; • the availability and cost of acquiring and shipping of supplies necessary for manufacturing and clinical trials; • the costs and timing of establishing sales, marketing, distribution and other commercial capabilities; • the terms and timing of establishing collaborations, license agreements and other partnerships; • costs associated with any new product candidates that we may develop, in- license or acquire; • the ~~effect~~ **effects** of competing technological and market developments; • our ability to establish and maintain partnering arrangements for development and / or commercialization; • the cost and timing of establishing enhanced internal

controls over financial reporting; and • the costs associated with being a public company. ~~Some of these factors are outside of our control.~~ We **may never generate the necessary data or results required to obtain regulatory approval in order to generate revenue from product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we** do not expect ~~our existing capital resources~~ to be ~~sufficient to enable us to fund the completion of our clinical trials and remaining development programs through commercial~~ **commercially** ~~introduction~~ **available for several years, if at all** . **Accordingly,** ~~We expect that~~ we will need **to continue to rely on additional financing to achieve our business objectives. We will need to raise substantial additional funding to finance our operations through clinical development of our product candidates and potentially to commercialize these candidates. We continue to analyze various alternatives, including public or private equity or debt financings, third- party funding, revenue interest arrangements, collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. Any additional fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our product candidates. We may experience difficulties in accessing the capital markets due to external factors beyond our control, such as volatility in the equity markets for emerging biotechnology companies and general economic and market conditions both in the U. S. and abroad. For example, our ability to raise additional capital may be adversely impacted by global economic conditions and disruptions to and volatility in the credit and financial markets in the U. S. and worldwide, such as have been experienced recently due in part to, among other things, the impacts of inflation, ongoing overseas conflicts, and disruptions in access to bank deposits and lending commitments due to bank failures. We may be unable** to raise additional funds ~~in~~ **or to enter into such agreements or arrangements on favorable terms, or at all. If we fail to obtain additional capital necessary to fund our operations, we could be forced to delay, limit, reduce or terminate our product development programs, commercialization efforts or** ~~the~~ **other** ~~future~~ **operations, or to cease operations or liquidate our assets** . ~~We~~ **Although we** have **been successful in raising capital in the past, there is** no ~~product candidate approved by any regulatory authority~~ **assurance that we will be successful in obtaining additional financing. Therefore** , ~~have not sold any products~~ **we cannot be certain that our plans to raise additional capital will be successful in alleviating the substantial doubt regarding our ability to continue as a going concern. Failure to manage discretionary spending or raise additional financing** , ~~and~~ **as needed, may adversely impact our ability to achieve our intended business objectives. If** we do not **obtain additional financing and are required to terminate our operations, our stockholders will lose all or a part of their investment. If we sell shares of our common stock or securities convertible into or exercisable for shares of our common stock in future financings or pursuant to licensing, collaboration or other arrangements, stockholders may experience immediate dilution and, as a result, our stock price may decline. Until such time, if ever, as we can generate substantial product revenues, we** expect to ~~sell~~ **finance** ~~or~~ **our** ~~derive~~ **cash needs through a combination of public or private equity or debt financings, third- party funding,** revenue ~~from any product sales for the foreseeable future. We may seek additional funding through, among other methods, collaboration agreements and public or private financings. Additional funding may not be available to us on acceptable terms or at all and the terms of any financing may adversely affect the holdings or the rights of our stockholders. General market conditions resulting from high~~ interest **arrangements** ~~rates, inflation, bank failures, domestic polities, global supply chain issues, and ongoing military conflicts~~ , as well as other **collaborations, strategic alliances and licensing arrangements or any combination of these approaches, grants, debt and other financings. We do not have any committed external source of funds. To the extent that we raise additional capital, if available, through the sale of equity or convertible debt securities, including through our " at- the-** market ~~conditions~~ **" offering program** , **the ownership interests of our existing stockholders will be diluted, and the terms of these securities** may **include liquidation** ~~make it difficult for . and the terms of these securities may include liquidation~~ or other preferences that adversely affect such holders' rights as a holder of our common stock.Debt **and revenue interest** financing,if available,may involve agreements that include covenants limiting or restricting our ability to take specific actions,such as incurring additional debt,making capital expenditures or declaring dividends or other distributions.Furthermore,we may issue common stock as consideration in acquisitions.If we issue common stock or securities convertible into common stock,our common stockholders would experience additional dilution and,as a result,our stock price may decline.If we raise additional funds through **collaborations,strategic alliances,third- party** licensing **arrangements** ~~,collaboration~~ or similar arrangements,we may have to relinquish valuable rights to our technologies,future revenue streams,research and development programs or product candidates or to grant licenses on terms that may not be favorable to ~~us~~ us **. If we are unable** to **raise** ~~obtain adequate~~ additional **funds through equity or debt** ~~financing~~ **financings or other arrangements** when needed **, we may be required to delay, limit, reduce or terminate** ~~or~~ **our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. The report of our independent registered public accounting firm for the year ended December 31, 2024 contains an explanatory paragraph regarding substantial doubt about our ability to continue as a going concern. Due to the uncertainty of our ability to meet our current operating and capital expenses, in the auditor' s report** on ~~attractive terms, or~~ **our audited annual financial statements as of and for the year ended December 31, 2024, our independent auditors included a paragraph regarding our ability to continue as going concern. Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock and we may have a more difficult time obtaining financing. Further, the perception that we may be unable to continue as a going concern may impede our ability to raise additional funds or operate our business due to concerns regarding our ability to discharge our contractual obligations. We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability. We have incurred significant operating losses since we were founded in 2006 and expect to incur significant losses for the foreseeable future as we continue development of our**

product candidates. Losses have resulted principally from costs incurred in our research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, regulatory compliance activities and, if any of our product candidates is approved, sales, marketing and other activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the next several years or longer. We currently generate no revenue from sales, and we may never be able to commercialize any of our product candidates. We do not currently have the required approvals to market any of our product candidates, and we may never receive such approvals. We may not be profitable even if we or any development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. **We are subject to risks associated with subletting our leased premises, including risks associated with subtenant defaults, which have occurred and we expect to continue to occur.** In ~~addition~~ **January 2021** , **we entered into an operating lease agreement for a building in North Carolina (" NC Premises ") and in October 2021, we entered into a sublease agreement with Jaguar Gene Therapy, LLC, (" Jaguar "), who subsequently assigned** the ~~issuance~~ **sublease to Advanced Medicine Partners, LLC (" AMP " or the " subtenant ") as the subtenant for the NC Premises, through the remainder** of ~~additional shares~~ **the lease term (ending in October 2037). Pursuant to the sublease and the notice and waiver of assignment (the " assignment agreement "), Jaguar remained obligated for AMP' s proper performance under the sublease. In February 2025, a lien in the amount of $ 4. 8 million was filed** by ~~us,~~ **a third- party contractor against the subtenant' s interest in the NC Premises. We discharged the lien in March 2025 by depositing cash in the full amount with the applicable court in order to avoid a default under the head lease. Further liens by third- party subcontractors** or ~~the~~ **other** ~~possibility of~~ **contractors have been or may in the future be filed against the subtenant' s interest in the NC Premises, and we may need to also discharge** such ~~issuance, may cause~~ **liens to avoid a default under** the ~~market price~~ **head lease. The subtenant and Jaguar failed to remit the March 2025 rent and subsequent rent payments and defaulted, and failed to cure such defaults, under the sublease and the assignment agreement for the NC Premises. As a result, we assumed responsibility for such payments in March 2025. As** of **April 7, 2025, we have made payments in the total amount of $ 1. 9 million to satisfy outstanding rent and common area management fee obligation, and we remain obligated under the head lease, including for all future remaining rent payments in an aggregate amount of up to $ 119. 7 million for the remainder of the head lease term, of which $ 5. 7 million is due between April 8 and December 31, 2025. As a result of the uncured defaults, we terminated the sublease and initiated a lawsuit against the subtenant and Jaguar in the Superior Court of Wake County, North Carolina to enforce our rights under the sublease and to seek recovery of losses and damages due to the defaults by the subtenant and Jaguar. In the event we are unsuccessful in collecting from the subtenant** ~~our~~ **or Jaguar or** ~~shares to decline. If we~~ are unable to obtain ~~funding~~ **a new subtenant** on **acceptable terms** ~~a timely basis, we may be unable to complete any current or future clinical trials for~~ **or at all,** ~~our product candidates and~~ we ~~may~~ **will** be required to **satisfy** ~~significantly curtail some or~~ **our obligations directly** ~~all of our activities. We also could be required~~ to ~~seek funds through arrangements~~ **the landlord under the head lease in accordance** with **its** ~~collaborative partners or otherwise that may require us to relinquish rights to our product candidates or some of our technologies or otherwise agree to~~ terms ~~unfavorable to us~~ . Risks Related to the Discovery and Development of Our Product Candidates Our business will depend substantially on the success of one or more of our product candidates. If we are unable to develop, obtain regulatory approval for, or successfully commercialize, any or all of our product candidates, our business will be materially harmed. We currently have one product candidate in clinical trials, and if that product candidate is not successful **,** our business could be materially impacted. Our other product candidates are in the early stages of development and will require substantial nonclinical and / or clinical development and testing, manufacturing process improvement and validation, clinical studies and regulatory approval prior to commercialization. It is critical to our business to successfully develop and ultimately obtain regulatory approval for one or more of these product candidates. Our ability to commercialize our product candidates effectively will depend on several factors, including the following: • successful completion of nonclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our product candidates; • receipt of marketing approvals for any future products for which we complete clinical trials, including securing regulatory exclusivity to the extent available; • establishing commercial manufacturing capabilities, for example, by engaging third- party manufacturers, partnering with a pharmaceutical licensee with manufacturing capabilities, or developing our own manufacturing capabilities that can provide products and services to support clinical development and the market demand for our product candidates, if approved; • successful launch and commercial sales of the product, whether alone or in collaboration with potential partners; • acceptance of the product as a viable treatment option by patients, the medical community and third- party payers; • establishing market share while competing with other therapies; • a continued acceptable safety profile of our products following regulatory approval; • maintaining compliance with post- approval regulations and other requirements; and • qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates. If we or our collaborators do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to commercialize our product candidates, which would materially and adversely affect our business, financial condition, results of operations and prospects. Of the large number of gene therapies, biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a ~~biologics license application (" BLA ")~~ to the FDA or marketing authorization application (" MAA ") to the European Medicines Agency (" EMA "), and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market any of our product candidates, any such approval may be subject to limitations on the indicated uses for which we may market the product, or limitations related to its distribution, or be conditional on future development activities and clinical results. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, there can be no

assurance that any of our product candidates will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval, or, if approved, successfully commercialize, any of our product candidates, we may not be able to generate sufficient revenue to continue **the operation of** our business **. In addition, difluprednate eye drops are not approved or commercially available in certain geographies where we intend or may choose to conduct Phase 3 clinical trials and to commercialize Ixo- vec, if approved, which could have an adverse effect on our ability to complete Phase 3 clinical trials or commercialize Ixo- vec in such jurisdictions or on our expected timelines** . Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials or any clinical trials using our proprietary viral vectors. Drug development has inherent risk. Our lead product candidate, ixoberogene soroparvovec (" Ixo- vec "), formerly referred to as ADVM- 022, for the treatment of wet age- related macular degeneration (" wet AMD "), uses a proprietary vector, AAV. 7m8, which has undergone limited human testing, and may generate unexpected results in clinical trials in the future, such as the dose- limiting toxicity at the 6 x 10 11 vg / eye (" 6E11 ") dose tested in the INFINITY trial in diabetic macular edema (" DME ") subjects. Although we will be bound by the generally applicable laws governing approval, the fact that Ixo- vec is a gene therapy and the broad patient population that it is intended to treat ~~means~~ **mean** that the safety and efficacy of our product and the related clinical data will be under increased scrutiny by competent authorities. There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia and death seen in other trials using other genomic therapies. Gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of significantly delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration that, while not necessarily adverse to the patient' s health, could substantially limit the effectiveness of the treatment. **Results in trials of competing product candidates or of other companies in our market sector may influence the perception of our product candidates. In addition, we may be adversely impacted if adverse events are reported for our or another party' s product or product candidate containing one of our proprietary viral vectors.** We, or any licensee or development partner, will be required to demonstrate through adequate and well- controlled clinical trials that our product candidate or another party' s product candidate containing one of our proprietary viral vectors is safe and effective for use in its target indications before seeking regulatory approvals for commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials or any clinical trials using our proprietary viral vectors. Any such delay or failure could significantly harm our business prospects, financial condition and results of operations. The occurrence of serious complications or side effects that outweigh the therapeutic benefit in connection with or during use of our product candidates, whether in nonclinical studies or clinical trials or post- approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post- approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business prospects, financial condition and results of operations. During the conduct of nonclinical studies and clinical trials, animal models and human subjects may experience changes in their health, including illnesses, injuries and discomforts. It is not always possible to accurately determine whether or not the product candidate being studied caused these conditions. In addition, subjects may not comply with the requirements of the study, such as missing physician visits or not taking eye drops as prescribed, which may result in changes to their health or vision that could then be attributed to the product candidate. Various illnesses, injuries, and discomfort may be reported from time- to- time in clinical trials of our product candidates. For example, a dose- limiting toxicity at the 6E11 dose tested in our INFINITY trial in DME subjects resulted in our announcement on July 22, 2021 that we were discontinuing development of Ixo- vec for the DME indication. It is possible that as we test Ixo- vec and other product candidates, in current and future clinical programs, or if use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomfort and other adverse events that were observed in earlier trials, including the dose- limiting toxicity at the 6E11 dose tested in the INFINITY trial, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. In some cases, side effects are only detectable after investigational products are tested in large- scale, Phase 3 clinical trials or later stage clinical trials, or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that one or more of our product candidates causes serious or life- threatening side effects, or side effects that outweigh the therapeutic benefit of the product candidate, the development of one or more of our product candidates may fail or be delayed, or, if one or more of our product candidates has received regulatory approval, such approval may be revoked, varied or suspended which would severely harm our business prospects, financial condition and results of operations. In order to understand the safety of our product candidates, when a subject experiences a negative health event during a clinical trial, we must determine if it is related to our product candidate. The subjects we enroll in our clinical trials for our current product candidates are generally less healthy than the general population, which increases the likelihood that a negative health event, unrelated to our product candidate, may occur. These health events may be misattributed to our product candidate, either by us, our investigators, or by regulators. Such misattribution could cause regulatory approval of our product candidates to be denied or delayed. For example, the subjects enrolled in our wet AMD trials are often geriatric and have other health conditions unrelated to wet AMD. We cannot assure you that we will be able to accurately determine whether or not a negative health event experienced by a subject in any of these or subsequent trials was related to Ixo- vec, nor can we assure you that the FDA or other regulatory authorities outside the U. S. responsible for reviewing the safety of Ixo- vec will agree with our determination. If a subject in one of our clinical trials experiences a negative health event, and that event is attributed to Ixo- vec, the trial and any other trials of Ixo- vec may be placed on clinical hold, and regulatory approval of Ixo- vec may be delayed or denied. In addition, if a subject enrolled in one of our clinical trials experiences a negative health event, the subject may be forced to

withdraw from our trial, or may become temporarily unavailable for follow- up visits, which may impact the amount or quality of data we obtain from our trial, which in turn may delay or prevent regulatory approval of our product candidate. Because subjects we enroll in our clinical trials for any of our product candidates are likely to be less healthy than the general population, and particularly in trials like OPTIC and LUNA that enroll a small number of subjects, this risk is increased. Our product candidates built on adeno- associated viral vector (" AAV ") vectors have similar risks to other gene therapy vectors, including inflammation, **pigmentary changes, including iris transillumination defects and anterior chamber pigmentation,** cytotoxic T- cell responses, anti- AAV antibodies and immune response to the transgene product, such as T- cell responses and / or antibodies against the expressed protein. For example, based on our current clinical experience, dose- related ~~intraocular~~ inflammation is a known side effect of Ixo- vec administration, but the duration of inflammation caused by Ixo- vec, our ability to prevent or manage that inflammation using corticosteroids or other anti- inflammatory or immunomodulatory treatments, and any potential clinical sequelae of that inflammation and treatments used to manage inflammation are not fully understood. Our LUNA trial is evaluating prophylactic corticosteroid regimens, including local corticosteroids and combinations of local and systemic corticosteroids to test the relative contribution of local versus systemic AAV exposure on ocular inflammation. In ~~February~~ **November** 2024, we announced LUNA **52- week** ~~preliminary safety and efficacy~~ data **with a cut- off date of August 29, 2024** . Ixo- vec was well- tolerated, and when present ~~intraocular~~ inflammation was responsive to per protocol local corticosteroids. ~~Preliminary~~ **Our 52- week** data suggest that ~~Ozurdex plus~~ difluprednate eye drops ~~may be~~ **alone are** a promising **" go forward"** prophylactic regimen for **our** future pivotal studies. The use of **a** ~~an Ozurdex plus~~ difluprednate eye drop prophylactic regimen may not be as successful in managing or mitigating inflammation in future, larger clinical trials or commercial use, and our reliance on the availability of these corticosteroids makes us vulnerable to drug shortage or other supply problems **. In addition, difluprednate eye drops are not approved or commercially available in certain geographies where we intend or choose to conduct Phase 3 clinical trials, which could have an adverse effect on our ability to complete Phase 3 clinical trials in these jurisdictions on our expected timelines** . Even if we achieve marketing approval, doctors may not prescribe, and patients may not use, Ixo- vec or our other product candidates if they deem the levels or risk of inflammation to be unacceptable or if they are unwilling or unable to use the required prophylactic corticosteroid regimen. Further, patients treated with Ixo- vec could develop antibodies against AAV. 7m8 capsid and / or aflibercept protein. These antibodies could preclude these patients from receiving other AAV- based gene therapies in the future. In addition, patients previously treated with or exposed to other AAV- based gene therapies could develop antibodies against AAV. 7m8 and / or the aflibercept protein, which could reduce or eliminate the effectiveness of Ixo- vec or could cause unanticipated adverse reactions to Ixo- vec. Studies have also found that intravenous delivery of certain AAV vectors at high doses may result in adverse events and have prompted the recommendation that studies involving high doses of AAV vectors should be monitored carefully for such adverse events. In addition, patients given infusions of any therapeutic protein or injection of gene therapies that **cause** ~~express~~ **expression of** a therapeutic protein may develop severe hypersensitivity reactions, infusion reactions, or serious side effects including transaminitis. With respect to our product candidates that are being or may be studied in diseases of the eye, there are additional potential serious complications related to IVT injection and taking aqueous fluid samples from the eye (" aqueous tap "), such as retinal detachment, endophthalmitis, ocular inflammation, cataract formation, glaucoma, damage to the retina or cornea, and bleeding in the eye. Serious complications or serious, unexpected side effects in connection with the use of our product candidates could materially harm our business prospects, financial condition and results of operations. Additionally, our lead product candidate, Ixo- vec, is designed for long- term, sustained expression of an exogenous protein, aflibercept. Even though Eylea ® (aflibercept) has been approved by several regulatory authorities, including the FDA, for the treatment of wet AMD, there may be side effects associated with aflibercept being expressed via a gene therapy treatment modality. If such side effects are serious or life threatening, the development of our product candidate and future product candidates may fail or be delayed, or, if such product candidate (s) have received regulatory approval, such approval may be revoked, which would severely harm our business prospects, financial condition and results of operation. The results of nonclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials may not have favorable results in later clinical trials, if any, or receive regulatory approval. If our product candidates are not shown to be safe and effective, we may not realize the value of our investment in our technology or product candidates. Promising nonclinical results generated with a product candidate in animal models do not guarantee similar results when the candidate is tested in humans. For example, the levels of protein expression achieved from a vector in a nonclinical model, including non- human primate models, may be significantly ~~higher~~ **different** than the level of protein expression achieved in humans. Similarly, human subjects administered our product candidates may develop side effects that were not observed in animal models and / or are more severe than those observed in animal models. In addition, even industry- accepted animal models may not accurately replicate human disease. Success in nonclinical studies or in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later- stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through nonclinical and initial clinical testing. Further, safety and / or efficacy issues with a product candidate may become apparent only when the product candidate is tested in human subjects suffering from the relevant disease. Furthermore, the initiation of future trials for a product candidate will be dependent upon demonstrating sufficient safety and efficacy to the relevant regulatory authorities in preceding or other ongoing trials using the same product candidate. We will still need to conduct Phase 3 pivotal trials in which we anticipate Ixo- vec will be compared to available therapies and utilize longer **-** term endpoints in order to support submission and approval of a BLA or equivalent outside of the U. S. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of products under development result in the submission of a marketing application and even fewer are approved for commercialization. Even if our clinical trials successfully meet their endpoints for safety and efficacy, the FDA and / or other regulatory authorities outside the U. S. may still conclude that the

product candidate has not demonstrated a beneficial benefit- risk profile or otherwise does not meet the relevant standard for approval. We cannot guarantee that results from any clinical trials that we plan will be successful, and any safety or efficacy 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. Our gene therapy platform is based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and the time, cost **,** and probability of subsequently obtaining regulatory approval. We have concentrated our research and development efforts on our gene therapy platform and in product candidates based on this platform, and our future success depends on the successful development of such product candidates. There can be no assurance that any development problems we have experienced or may experience in the future related to our platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to external commercial manufacturing sites, which may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all. In addition, the clinical trial requirements of the FDA, EU competent authorities and other regulatory authorities outside the U. S. and the criteria these regulators may use to determine the quality, safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential ~~products~~ **product** . The regulatory approval process for novel gene therapy products such as ours can be more expensive and take longer than for other treatment modalities, which are better known or more extensively studied to date. To date, approvals for gene therapy products by the FDA have been generally for rare diseases with limited treatment options. Because we are targeting a broad population of patients with wet AMD, for which there ~~is an~~ **are multiple** approved and widely adopted standard **-** of **-** care **therapies** , the benefit- risk profile of Ixo- vec may be subject to greater scrutiny by regulatory authorities. Regulatory approaches and requirements for gene therapy products continue to evolve, and any changes could create significant delay and unpredictability for product development and approval as compared to technologies with which regulatory authorities have more substantial experience, including, for example, reevaluating whether to require a companion diagnostic for gene therapy products. Before a clinical trial can begin to enroll at a clinical site, the site' s Institutional Review Board (" IRB ") **or Ethics Committee** and its Institutional Biosafety ~~Committee, or Ethics~~ Committee must review the proposed clinical trial to assess the appropriateness to conduct the clinical trial at that site. In addition, adverse events in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory authorities outside the U. S. to change the requirements for human research on or for approval of any of our product candidates. These regulatory authorities, review committees and advisory groups, and the guidelines they promulgate, may lengthen our regulatory review process, require us to perform additional studies, increase our development costs, increase or otherwise change chemistry, manufacturing, and controls requirements, lead to changes in our 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 usually be required to consult with these, and potentially other, regulatory and advisory groups and comply with applicable guidelines or recommendations. If we fail to do so or the consultations take longer than we expect, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs incurred in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. Identifying and qualifying patients to participate in our clinical trials will be critical to our success. The timing of current and future clinical trials will depend on the speed at which we can recruit patients to participate in future testing of these product candidates. We have in the past and may in the future experience difficulties or delays enrolling patients in our clinical trials. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials, clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating and patient' s safety concerns over participating in a clinical trial. We will be required to identify and enroll a sufficient number of patients for any clinical trial for our product candidates. Potential patients may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our trials. Additionally, some patients may **meet exclusion criteria** ~~have neutralizing antibodies at titer levels~~ that would prevent them from being enrolled in a clinical trial for any of our product candidates ~~, or may meet other exclusion criteria~~ . As a consequence, enrollment in our clinical trials may be limited or slowed. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for such future clinical trials. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial. We plan to seek initial marketing approval of our product candidates in the U. S. **, EU** and / or ~~the~~ **other** ~~EU~~ **countries** and we may not be able to successfully conduct clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, the EU or other regulatory authorities outside the U. S. In addition, the process of finding and diagnosing patients may prove costly. Further, if patients and investigators are unwilling to participate in our gene therapy studies because of the dose-limiting toxicity at the 6E11 dose tested in the INFINITY trial, ~~because of~~ negative publicity from other adverse events in the biotechnology or gene therapy sector, inadequate results in our nonclinical studies or clinical trials, or for other reasons, including competitive clinical trials for similar patient populations or available approved therapies, our recruitment of patients, or conduct of clinical trials and ability to obtain regulatory approval of our product candidates may be hindered. Trials using early versions of retroviral vectors, which integrate into, and thereby alter, the host cell' s DNA, have led to several well-publicized adverse events. Our product candidates use an AAV delivery system, with which host integration has been less of a concern. Nonetheless, if patients negatively associate our product candidates with the adverse events caused by previous gene

therapy products, they may choose not to enroll in our clinical trials, which would have a material adverse effect on our business and operations. If we have difficulty enrolling a sufficient number of patients to conduct clinical trials on our product candidates as planned, we may need to delay, limit or terminate future clinical trials, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Our product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates. The nonclinical and clinical development, manufacturing, analytical testing, labeling, storage, record- keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA and by comparable regulatory authorities outside the U. S. In the U. S., we are not permitted to market our product candidates until we receive regulatory approval from the FDA. Similar approvals are required to market our product candidates outside of the U. S. The process of obtaining regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved, as well as the target indications and patient population. Approval policies or regulations may change, and the regulatory authorities have discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. The FDA or comparable regulatory authorities outside the U. S. can delay, limit or deny approval of a product candidate for many reasons, including: • such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials; • we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities outside the U. S. that a product candidate is safe and effective for any indication; • the FDA or other regulatory authorities outside the U. S. may not accept clinical data from trials which are conducted at multinational clinical facilities or in countries where the standard of care is potentially different from that of the U. S. or the other regulatory authorities outside the U. S.; • the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval; • we or any of our future development partners may be unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; • such authorities may disagree with our interpretation of data from nonclinical studies or clinical trials; • approval may be granted only for indications that are significantly more limited than what we apply for and / or with other significant restrictions on distribution and use; • such authorities may find deficiencies in our manufacturing processes, analytical testing, or facilities or in the manufacturing processes, analytical testing or facilities of third- party manufacturers or testing laboratories with which we or any of our future development partners contract for clinical and commercial supplies; ~~or~~ • the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval **; or • approval from such authorities may be conditioned on the collection of additional data or otherwise contain significant post- marketing obligations** . With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of related products, including those already on the market, may result in increased cautiousness by the FDA and comparable regulatory authorities outside the U. S. in reviewing our product candidates based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates. Preliminary and interim data from our clinical trials that we may announce or publish from time to time may change as each clinical trial progresses. From time to time, we may announce or publish preliminary or interim data from our clinical trials. Preliminary and interim results of a clinical trial are not necessarily predictive of final results. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change as subject enrollment continues or further subject follow up occurs and more subject data become available. In addition, in certain clinical trials, such as our OPTIC trial, individual cohorts of subjects were enrolled with different dosages and other treatment conditions under our protocol. These different doses, populations, and other treatment conditions may affect clinical outcomes, including safety profiles or efficacy, such as the number of supplemental injections required, in each of the cohorts. As a result, preliminary and interim data should be viewed with caution and not relied upon until the final data from a locked database for the entire clinical trial are available. Material changes in the final data compared to preliminary or interim data could significantly harm our business prospects. Fast Track **and Regenerative Medicine Advanced Therapy (" RMAT ")** ~~designation~~ **designations** by the FDA, PRIME designation by the EMA and the Innovation Passport by the MHRA for Ixo- vec may not lead to a faster development, regulatory review or approval, and they do not increase the likelihood that Ixo- vec will receive marketing approval in the U. S. We received Fast Track designation for Ixo- vec in September 2018 for the treatment of wet AMD. The FDA may grant Fast Track designation to a drug that is intended to treat a serious condition and nonclinical or clinical data demonstrate the potential to address an unmet medical need. The FDA provides opportunities for frequent interactions with the review team for a Fast Track product, including pre- investigational new drug application (" IND ") meetings, end- of- phase 1 meetings, and end- of- phase 2 meetings to discuss study design, extent of safety data required to support approval, dose- response concerns, and use of biomarkers. A Fast Track product may also be eligible for **Priority Review and** ~~rolling~~ **Rolling Review, which may potentially result in a shorter FDA** review **process. In July 2024** , ~~where the~~ FDA **granted RMAT designation for Ixo- vec for the treatment of wet AMD. An investigational drug product is eligible for the RMAT designation if: (1) it meets the definition of a regenerative therapy medicine, which includes cell therapies, therapeutic tissue engineering products, human cell and tissue products, or combination products using such therapies or products, with limited exceptions; (2) the product is intended to treat, modify, reverse, or cure a serious disease or condition; and (3) preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such disease or condition. RMAT designation offers potential benefits that include increased collaboration with the FDA to accelerate development**

including the potential for Priority ~~reviews -~~ **Review** ~~portions of a marketing application before the sponsor submits the complete application -~~. The EMA granted Ixo- vec Priority Medicines (“ PRIME ”) designation in June 2022 for the treatment of wet AMD. PRIME is a program launched by the EMA to enhance support for research on and development of medicines that have demonstrated the potential to target a significant unmet medical need on the basis of data showing a meaningful improvement of clinical outcomes. This regulatory program offers **sponsors** ~~developers of medicines -~~ enhanced interaction and early dialogue with the EMA and is designed to optimize development plans and speed evaluation ensuring these medicines reach patients as early as possible. The United Kingdom’ s MHRA granted Ixo- vec an Innovation Passport under the Innovative Licensing and Access Pathway (“ ILAP ”) in April 2023. ILAP is a ~~new~~ pathway supporting innovative approaches to the safe, timely, and efficient development of medicines aiming to accelerate the time to market, facilitating patient access to medicines. ~~The~~ ILAP ~~Is~~ **is** comprised of ~~an~~ **the** Innovation Passport designation ~~,~~ **and** a Target Development Profile and provides applicants with access to a toolkit to support the design, development and approvals process. The Innovation Passport is the first step in the ILAP process, triggering the MHRA and its partner agencies, including the All Wales Therapeutics and Toxicology Centre, the National Institute for Health and Care Excellence, and the Scottish Medicines Consortium to partner with Adverum to charter a roadmap for regulatory and development milestones with the goal of early patient access in the United Kingdom (“ UK ”). However, Fast Track **, RMAT** , PRIME and ILAP designations for Ixo- vec may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and ~~does~~ **do** not assure ultimate approval by the FDA, the European Commission, or MHRA. In addition, the FDA and MHRA can rescind or revoke the designations for Ixo- vec if the regulatory agencies later determine that Ixo- vec no longer meets the qualifying criteria for ~~each~~ **such** designation. The EMA can remove Ixo- vec from the PRIME eligibility list if Ixo- vec no longer meets the eligibility criteria. We may not be successful in our efforts to identify or discover additional product candidates. The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our platform technology. Our research programs may fail to identify other potential product candidates for clinical development for a number of reasons. For example, our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to lack efficacy, have harmful side effects, or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that may ultimately prove to be unsuccessful. Risks Related to Manufacturing If we are unable to successfully develop and maintain robust and reliable manufacturing processes for our product candidates, we may be unable to advance clinical trials or licensure applications and may be forced to delay or terminate a program. The development of commercially viable manufacturing processes typically is very difficult to achieve, is often very expensive and may require extended periods of time. As we develop, seek to optimize, and operate the Ixo- vec manufacturing process, internally **and /** or through third parties **such as CMOs or potential partners** , we will likely face technical and scientific challenges, considerable capital costs, and potential difficulty in recruiting and hiring experienced, qualified personnel. There may also be unexpected technical or operational issues during clinical manufacturing campaigns or process validation campaigns. For example, all Good Manufacturing Practices (“ GMP ”) activities **, whether conducted** at our Redwood City facility, ~~and~~ **or by** external manufacturing, testing, and distribution **vendors or potential** partners are subject to significant health authority regulation with respect to manufacturing and testing our product candidates. If we are unable to satisfy these regulatory requirements, or if we are unable to solve the technical, scientific, and other challenges described above, we may be unable to manufacture a sufficient supply of our product candidates for our clinical trials and may be forced to delay or terminate our development programs. Additionally, changes in manufacturing processes (including cell lines and viral banks), equipment or facilities (including moving manufacturing or testing from one of our facilities to another one of our facilities or a third- party facility, **such as CMOs or potential partners,** or from a third- party facility **, such as CMOs or potential partners,** to one of our facilities) may require us to conduct additional studies to demonstrate comparability in order to receive regulatory approval of any manufacturing modifications. As a result, we could experience manufacturing delays that prevent us from commencing or completing our clinical studies on the timelines we anticipate, if at all. We may revise the process that we use to manufacture Ixo- vec for clinical trials. Before we use a revised process in clinical trials, we must submit analytical comparability data to the FDA and comparable regulatory authorities outside the U. S. to demonstrate that the process changes have not altered Ixo- vec in a manner that undermines the applicability of the clinical data from our clinical trials. If the FDA and comparable regulatory authorities outside the U. S. do not find our analytical comparability data sufficient, the FDA and comparable regulatory authorities outside the U. S. could place our IND or equivalent on clinical hold until we conduct additional nonclinical or clinical comparability studies demonstrating that the Ixo- vec manufactured by our revised process and our previous process are materially equivalent, which could substantially delay the development process. If we make further changes to the manufacturing process, equipment or facilities of Ixo- vec in the future, the FDA and comparable regulatory authorities outside the U. S. may require us to demonstrate comparability between Ixo- vec manufactured before and after the change. For example, the FDA and comparable regulatory authorities outside the U. S. could require comparability studies to demonstrate that Ixo- vec manufactured in its current facilities is comparable to Ixo- vec manufactured at future commercial supply sites, which could delay our commencement or completion of clinical trials. We do not know whether any required comparability studies will begin as planned, will need to be restructured or will be completed on schedule, or at all. If the results of these comparability studies are not positive or are only modestly positive or if there are safety concerns, we may be delayed in obtaining marketing approval for Ixo- vec or not obtain marketing approval at all. Our product development costs **will** also ~~will~~ increase if we experience delays in testing or regulatory approvals. If we are unable to produce sufficient quantities of our products and

product candidates at acceptable costs, we may be unable to meet clinical or potential commercial demand **, face delayed timelines** , lose potential revenue, have reduced margins, or be forced to terminate a program. Due to the complexity of manufacturing our products, we may not be able to manufacture sufficient quantities to meet clinical or potential commercial demand. Our inability to produce enough of a product meeting all release acceptance criteria at acceptable costs may cause us to be unable to meet clinical or potential commercial demand **, to delay our clinical and / or commercialization timelines** , to lose potential revenue, to have reduced margins, or to be forced to discontinue such product. As we develop, seek to optimize and operate the Ixo- vec manufacturing process internally or through third parties, we will likely face technical and scientific challenges, considerable costs, and potential difficulty in recruiting and hiring experienced, qualified personnel. We have in the past and may in the future experience unexpected technical or operational issues during clinical or commercial manufacturing campaigns. As a result, we could experience manufacturing delays that prevent us from commencing or completing clinical studies or commercializing Ixo- vec, if approved, on a profitable basis, if at all. In addition, our manufacturing processes will subject us to a variety of U. S. federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of hazardous materials and wastes resulting from their use, as well as comparable legislation and regulations outside of the U. S. We will incur significant costs in complying with these laws and regulations. Gene therapy products are novel and complex and have only in limited cases been manufactured at scales sufficient for pivotal trials and commercialization. Few pharmaceutical contract manufacturers specialize in gene therapy products and those that do are still developing appropriate processes and facilities for large- scale production. If we are unable to secure adequate manufacturing capacity from our contract manufacturing partners, or if our contracted slots are canceled or delayed in order to prioritize other projects, we may be unable to produce sufficient quantities of our product candidates for our development programs and for commercialization. Changes in methods of manufacturing or formulation of our product candidates may result in additional costs or delays. As our product candidates progress through preclinical to late- stage clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods ~~and~~ **,** formulation, and manufacturing sites are altered along the way in an effort to optimize yield and manufacturing batch size, reduce costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of **our ongoing and** planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue. We and our contractors are subject to significant regulation with respect to manufacturing and testing our product candidates. We have a limited number of vendors on which we rely, including, in some cases, single source vendors, and the contract vendors on which we rely may not continue to meet regulatory requirements, may have limited capacity, or may have other factors limiting their ability to comply with their contracts with us. We currently have relationships with a limited number of suppliers for the manufacturing and testing of our vector product candidates. Our suppliers may require licenses to manufacture or test such components if such processes are not owned by the suppliers or in the public domain ~~,~~ and ~~we~~ may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities, and may be unable to acquire such rights, to the extent that we do not already have them. All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract vendors for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product used in clinical trials or approved for commercial sale must be manufactured and tested in accordance with GMP regulations. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis **. If we or a contract manufacturer are unable to do so, we may experience clinical or commercialization delays or be required to expend significant resources to work with** ~~and~~ **an alternative contract manufacturer. We and our contract manufacturers** must **also** adhere to the FDA' s GMP regulations enforced by the FDA through its facilities inspection program as well as other comparable regulations enforced by other regulatory authorities outside the U. S. Our contract manufacturers have not produced a commercially ~~-~~approved AAV product and therefore have not yet demonstrated compliance with GMP regulations to the satisfaction of the FDA or other regulatory authorities outside the U. S. Our facilities and quality systems and the facilities and quality systems of some or all of our third- party contractors must pass a pre- approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. If the facility does not pass a pre- approval plant inspection, the FDA or other regulatory approval of the products will not be granted. In addition, the regulatory authorities may, at any time, audit or inspect any manufacturing facility we may have or those of our third- party contractors involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Should the FDA or other regulatory authorities outside the U. S. determine that the facility is not in compliance with applicable regulations, the manufacture and release of our product candidates may not be possible, and our business could be harmed. The regulatory authorities also may, at any time, inspect any manufacturing facility we may have or those of our third- party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if we become aware of a violation of our product specifications or applicable regulations, independent of an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and / or time- consuming for us or a third **-** party to implement and which may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Such violations could also result in civil and / or criminal penalties. Any such remedial measures or other civil and / or criminal

penalties imposed upon us or third parties with whom we contract could materially harm our business. If we or our third- party contractors fail to maintain regulatory compliance, the FDA or other regulatory authorities outside the U. S. can impose regulatory sanctions including ~~,~~ shutdown of the third- party vendor or invalidation of drug product lots or processes, fines, injunctions, civil penalties, delays, suspension, variation or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products, if approved, and significantly harm our business, financial condition, results of operations and prospects. Additionally, if the service provided by an approved manufacturing or testing contractor is interrupted, there could be a significant disruption in commercial supply. Alternative contractors could need to be qualified through a BLA supplement **,** which could result in further delay. The regulatory authorities may also require additional studies showing comparability between approved product or testing ~~,~~ and **the** product or testing provided after a contractor change, if a new manufacturing or testing contractor is relied upon for commercial production. Changing contractors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, causing us to incur higher costs, and preventing us from commercializing our product candidates successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed, or we could lose potential revenue. We may face difficulties from changes to current regulations and future legislation. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U. S. or abroad. The policies of the FDA, the competent authorities of the EU Member States, the EMA, the European Commission and other comparable regulatory authorities responsible for clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation ~~, or~~ **(“** CTR **”)** , which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each EU Member State, leading to a single decision for each EU Member State. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment by all EU Member States concerned, and a separate assessment by each EU Member State with respect to specific requirements related to its own territory, including ethics rules. Each EU Member State’ s decision is communicated to the sponsor via the centralized EU portal. Once the clinical trial approved, clinical study development may proceed. The CTR ~~foresees~~ **foresaw** a three- year transition period **that ended** ~~. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials in relation to which application for approval was made~~ on ~~the basis of the Clinical Trials Directive before~~ January 31, ~~2023, the Clinical Trials Directive will continue to apply on a transitional basis until January 31,~~ 2025. ~~By that~~ **Since this** date, all **new or** ongoing trials **are** ~~will become~~ subject to the provisions of the CTR ~~. The CTR will apply to clinical trials from an earlier date if the related clinical trial application was made on the basis of the CTR or if the clinical trial has already transitioned to the CTR framework before January 31, 2025~~ . Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. In addition, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation **and on April 10, 2024, the Parliament adopted its related position. The proposed revisions remain to be agreed and adopted by the European Council. Moreover, on December 1, 2024, a new European Commission took office. The proposal could, therefore, still be subject to revision** . If adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity opportunities for our product candidates in the EU and make them open to generic or biosimilar competition earlier than is currently the case with a related reduction in reimbursement status. The United Kingdom’ s withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business. **Following Brexit** ~~On January 31, 2020~~ , the UK **and** ~~withdrew from~~ the ~~European Union (“~~ EU **signed a EU- ”**~~), commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the~~ UK ~~and the EU, the UK was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply. The UK- EU~~ Trade and Cooperation Agreement, which **became provisionally applicable on January 1** ~~has applied since the end of the Transition Period~~ , **2021 and entered into force on May 1, 2021. This agreement** provides ~~for tariff~~ **details on how some aspects of the UK and EU’ s relationship will operate going forwards however there are still uncertainties. The EU - UK Trade and Cooperation Agreement primarily focuses on ensuring** free trade ~~of~~ **between the EU and the UK in relation to** goods, **including** ~~but not services, between the UK and the EU, but there may however be additional non- tariff costs which did not exist prior to the end of the Transition Period. Further, should the UK further diverge from the EU from a regulatory perspective in relation to medical products, tariffs could be put into place in the future. Although the body of the UK- EU Trade and Cooperation Agreement includes general terms which apply to~~ medicinal products ~~, greater detail on sector- specific issues is provided in an Annex to the Agreement~~ . **Among** ~~The Annex provides a framework for~~ the ~~recognition of GMP inspections and for the exchange~~ ~~--~~ **changes that have occurred are that the UK** ~~and acceptance of official GMP documents. The regime does not, however, extend to procedures such as batch release certification, and Great Britain (England, Scotland and Wales)~~ is treated as a **“** third country ~~.~~ **”, a country that is not a member of the EU and whose citizens do not enjoy the EU right to free movement (** Northern Ireland ~~, has continued~~ **continues** to follow **certain limited** EU regulatory rules, **including in relation to medical devices,** but ~~pursuant to the Windsor Framework, a post- Brexit legal agreement entered into between the EU and UK Northern Ireland will no~~ **not in relation** ~~longer be subject~~ to **medicinal products)** ~~EU Regulations as of January 1, 2025~~ . As part of the **EU-** UK ~~- EU~~ Trade and Cooperation Agreement, the EU and the UK ~~will~~ recognize GMP inspections carried out by the other ~~Party~~ **party** and the acceptance of official GMP documents issued by the other ~~Party~~ **party** . The **EU-** UK ~~- EU~~ Trade and Cooperation Agreement also encourages, although it does not oblige, the parties to consult one another on

proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The UK ~~continues~~ **has unilaterally agreed** to accept EU batch testing and batch release ~~, but has recently conducted a consultation as to the future strategy for batch testing policy; two years notice will be provided of any change to such a policy~~ . However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. **This means that medicinal products that are tested and released in the UK must be retested and re- released when entering the EU market for commercial use. On February 27, 2023, the UK Government and the European Commission reached a political agreement on the so- called " Windsor Framework ". The Windsor Framework is intended to revise the Northern Ireland Protocol to address some of the perceived shortcomings in its operation. The agreement was adopted at the Withdrawal Agreement Joint Committee on March 24, 2023 and the arrangements under the Windsor Framework relating to medicinal products took effect on January 1, 2025.** As ~~regards~~ **it relates to** marketing authorizations, ~~Great Britain~~ **the United Kingdom** has a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland ~~has~~ continued **, until January 1, 2025** to be covered by ~~centralized~~ **the** marketing authorizations granted by the European Commission ~~(" EC ").~~ but the Windsor Framework provides that the UK MHRA **is** ~~will be~~ the sole regulatory body responsible for granting marketing authorizations for Northern Ireland as of January 1, 2025. ~~There are currently delays on cross- border trade between the UK and the EU as businesses and governmental bodies adapt to the arrangements. We and our contract vendors currently rely on other contractors based in the UK. The implementation of new governmental policies associated with Brexit may affect our UK- based contractors' ability to comply with applicable regulations, including existing EU regulations. If they are unable to return to compliance, or if an acceptable substitute vendor cannot be identified, it may negatively impact our business. Further, to the extent that our UK- based contractors have supply relationships with vendors in the EU, these contractors may experience difficulties, delay or increased costs in receiving materials from their vendors in the EU, which could have a material adverse effect on our UK- based contractors' ability to provide the services or materials to us.~~ A significant proportion of the regulatory framework in the UK applicable to medicinal products is currently derived from EU Directives and Regulations. The potential for UK legislation to diverge from EU legislation following Brexit could materially impact the regulatory regime with respect to the development, manufacture, import, approval, and commercialization of our product candidates in the UK or the EU. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. All of these changes could increase our costs and otherwise adversely affect our business. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the UK or the EU and restrict our ability to generate revenue and achieve and sustain profitability. In addition, we may be required to pay taxes or duties or be subjected to other hurdles in connection with the importation of our product candidates into the EU. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK or the EU for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import / export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non- tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU. We are subject to many manufacturing and distribution risks, any of which could substantially increase our costs and limit supply of our product candidates. The process of manufacturing our product candidates is complex, highly regulated and subject to several risks, including: • Due to the complexity of manufacturing our product candidates, we may not be able to manufacture sufficient quantities to support our clinical trials. Delays in manufacture and supply by our contract manufacturing partners may also cause delays in their ability to supply the amount of our product that we have ordered and on which we have based our expected development timelines. Our inability to produce enough of a product candidate at acceptable costs may result in the delay or termination of development programs. • The manufacturing and distribution of biologics is extremely susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, or transportation or storage conditions of the product. Even minor deviations from prescribed manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other ~~contaminations~~ **contamination** ~~are~~ **is** discovered in our product candidates or in ~~the~~ **a** manufacturing facility in which our product candidates are made, such manufacturing facility may need to be closed for an extended period of time to investigate and remedy the contamination. • The manufacturing facilities in which our product candidates are made could be adversely affected by equipment failures, labor shortages, contaminants, raw materials shortages, natural disasters, power failures, and numerous other factors. • We and our contract manufacturers must comply with the FDA' s and comparable foreign regulatory authorities' GMP regulations and guidelines. We and our contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our contract manufacturers are subject to inspections by the FDA and comparable regulatory authorities in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow GMP or other regulatory requirements or any delay, interruption, or other issues that arise in the manufacture, fill- finish, packaging, storage, or distribution of our product candidates as a result of a failure of our facilities, or the facilities or operations of third parties, to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our product candidates. This may lead to significant delays in the availability of sufficient supply of the product candidate substance for our clinical trials or the termination or hold on a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our product candidates. • Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals

for our product candidates, delays, suspension, variation or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions, and criminal prosecutions, any of which could be costly and damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our product candidates, if approved, and / or may be subject to product recalls, seizures, injunctions **,** or criminal prosecution. • Our product candidates are biologics and require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be adequately characterized prior to manufacturing the final product. As a result, an assay of the finished product is not sufficient to ensure that the product will perform in the intended manner. Accordingly, we expect to employ multiple steps to attempt to control our manufacturing process and assure that the product or product candidate is made strictly and consistently in compliance with the process. • We continue to develop the manufacturing process ~~for late- stage clinical product~~ , and our current process has not been fully characterized and therefore is open to potential variations that could lead to defective product substance that does not meet specification. • Problems with the manufacturing, storage or distribution of our product candidates, including even minor deviations from our established parameters, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory. • Some of the raw materials required in our manufacturing process are derived from biological sources. Such raw materials are difficult to procure and may also 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 commercialization. Any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our product candidates, which could affect the timing of our commencement and completion of clinical studies. We may also have to take inventory write- offs and incur other charges and expenses for product that fails to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives. We may encounter problems manufacturing sufficient research-, clinical-, or commercial- grade materials that meet FDA, EU or other applicable standards or specifications with consistent and acceptable production yields and costs. Risks Related to Our Reliance on Third Parties We have relied, and expect to continue to rely, on third parties under contracts and partnerships to conduct some or all aspects of our research and development, including vector production, process development, assay development, product candidates and product manufacturing and testing, protocol development, clinical trials, product distribution, commercialization, nonclinical studies, research and related activities, and these third parties may not perform satisfactorily. We do not expect to independently conduct all aspects of our vector production, product and product candidate manufacturing and testing, protocol development, clinical trials, product distribution, commercialization, nonclinical studies, research and related activities. We currently rely, and expect to continue to rely, on third parties with respect to these items. We may not be able to enter into agreements or partnerships with these third parties and if we do enter into agreements with these third parties, we cannot be assured these agreements will be on favorable economic terms or that any of these third parties will be successful at fulfilling their contractual obligations, and it is possible they may choose to terminate their engagements with us. If we need to enter into alternative arrangements, it could delay or jeopardize our product development activities **or regulatory filings** or be more costly. Our reliance on these third parties for vector production, process development, assay development, product and product candidate manufacturing and testing, protocol development, clinical trials, product distribution, commercialization, nonclinical studies, research and related activities ~~will reduce~~ **reduces** our control over these activities but ~~will~~ **does** not relieve us of our responsibility to ensure compliance with all required regulations. If any of these third parties on which we rely do not perform satisfactorily, we will remain responsible for ensuring that: • each of our nonclinical studies and clinical trials are conducted in accordance with the study plan and protocols and applicable regulatory requirements; • vector production, product and product candidate manufacturing and testing are conducted in accordance with applicable GMP requirements and other applicable regulatory requirements; and • other research, process development, and assay development are conducted in accordance with applicable industry and regulatory standards and norms; any of which we may not be able to do. We will continue to rely on third- party manufacturers and suppliers, and may enter into partnerships and other business development arrangements, which ~~entails~~ **entail** risks, including: • the inability to negotiate manufacturing, supplier agreements, partnerships or other agreements with third parties under commercially reasonable terms; • reduced control as a result of using third- party manufacturers or partners for some or all aspects of manufacturing activities; • termination or nonrenewal of manufacturing agreements, partnerships, or supplier 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 or suppliers caused by conditions unrelated to our business or operations, including the acquisition, change in control, or bankruptcy of the manufacturer, supplier or partner, or their commitments to other vaccine and therapeutics production projects that may reduce available manufacturing capacity. Any of these events could lead to clinical trial delays, failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. We **rely and** will **continue to** rely on third parties to conduct some nonclinical testing and all of our **ongoing and** planned clinical trials. If these third parties do not meet our deadlines or otherwise fail to conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all. We do not have the ability to conduct all aspects of our nonclinical testing, clinical testing, or clinical trials ourselves. We are dependent on third parties to conduct nonclinical studies and clinical trials for our product candidates, and, therefore, the timing of the initiation and completion of these studies or trials is controlled in part by these third parties and may occur at times substantially different from our estimates. Specifically, we use and rely on medical institutions, clinical investigators, contract research organizations (“ CROs ”) and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data. There is no guarantee that any CROs, investigators or other third parties on which we rely for administration and conduct

of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, fails to meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow- up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the utility of certain data from the clinical trial may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any IND or BLA we submit to the FDA, or equivalent submissions to other regulatory authorities outside the U. S. Any such delay or rejection could prevent us from commercializing our product candidates. Risks Relating to Our Intellectual Property Our success depends on our ability to protect our intellectual property and our proprietary technologies. 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. There can be no assurance that any of our product candidates will have patent protection, that our patent applications or those of our licensors will result in patents being issued or that issued patents, if any, will afford sufficient protection against competitors with similar technology, nor is there any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. 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. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our business, financial condition, results of operations and prospects. We own and license certain composition- of- matter patents and applications covering components of our product candidates. Composition- of- matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our patent applications covering composition- of- matter of any of our product candidates will be considered patentable by the U. S. Patent and Trademark Office (“ USPTO ”) and courts in the U. S. or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition- of- matter patents will not be found invalid or unenforceable if challenged. We own and license certain method- of- use patents and applications covering methods of treating certain diseases with our product candidates. Method- of- use patents protect the use of a product for the specified method or for treatment of a particular indication. However, methods of treating human diseases are considered unpatentable in many jurisdictions, and even where available this type of patent does not prevent a competitor from making and marketing a product that is identical to our product candidate for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “ off- label. ” Although off- label prescriptions may infringe or contribute to the infringement of method- of- use patents, the practice is common and such infringement is difficult to prevent or prosecute. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following: • 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. 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; • 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; • patents may expire before or soon after the product they cover is commercialized; • 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 product candidates; • 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 U. S. for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and • countries other than the U. S. may have patent laws less favorable to patentees than those upheld by the U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates. In addition, we rely on the protection of our trade secrets and know- how. Although we have taken steps to protect our trade secrets and know- how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. Trade secrets do not provide any protection against the independent development of the trade secret by a competitor or other third - party. If a competitor independently obtains or develops our trade secret, either by reverse engineering our product or other legal means, we would be unable to prevent them from using the trade secret, and our competitive position would be harmed. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know- how, the value of this information may be greatly reduced. Our reliance on third parties requires us to share our trade secrets and other confidential information, which increases the possibility that a competitor will discover them or that our confidential information, including trade secrets, will be

misappropriated or disclosed. Because we rely on third parties to conduct research and to develop and manufacture our product candidates, we must, at times, share confidential information, including trade secrets, with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements containing confidentiality provisions 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 they become known by our competitors, are purposefully or inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Public disclosure of our confidential information also prevents us from seeking patent protection for that or related discoveries. Given that our proprietary position is based, in part, on our know- how and trade secrets, the unauthorized use or disclosure of our trade secrets would impair our competitive position and may have a material adverse effect on our business, financial conditions, results of operations and prospects. In addition, these agreements typically restrict the ability of our advisors, employees, third- party contractors and consultants to publish data potentially relating to our confidential information and trade secrets, although our agreements may contain certain limited publication rights. For example, academic institutions that we collaborate with often require rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential information or trade secrets from any such publication. However, we may fail to recognize or identify to our collaborator such confidential information or trade secrets during the appropriate timeframe prior to publication, and they may be publicly disclosed without us filing for patent or other protection. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, including through breach of our agreements with third parties, failure of our security measures or publication of information by any of our third- party collaborators, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know- how and inventions. A competitor' s discovery of our trade secrets could impair our competitive position and have an adverse impact on our business, financial condition, results of operations and prospects. 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. The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands, especially in the field of gene therapy, 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. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third- party patents that may be infringed by commercialization of our product candidates. 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 to defend against 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; or • require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all. Others may hold proprietary rights that could prevent our product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market our product candidates. 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. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. 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, which could harm our business, financial condition, results of operations and prospects. We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in- licenses. We currently have rights to 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 may depend in part on our ability to acquire, in- license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in- license any compositions, methods of use, processes, or other 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 sometimes collaborate with U. S. and foreign academic institutions to accelerate our research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to 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, financial condition, results of operations and prospects could be materially and adversely affected. Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies and universities. We currently are heavily reliant upon licenses of certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide adequate rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future, or may contain other limitations on our ability to use such intellectual property or technology. As a result, our ability to develop or commercialize our processes and product candidates may be limited by the terms of such agreements. Further, the third parties from whom we license certain patent rights and proprietary technology **have in the past attempted and** may **in the future** attempt to terminate their agreements with us. **We** ~~For example, in 2019 we received from Virovek a notice of intent to terminate our non- exclusive license to certain Virovek technology and know- how related to methods and materials for manufacturing adeno- associated virus. Although no further action has been taken in that matter, it illustrates that if one of our licenses were to be terminated, we~~ may be unable to obtain a new license to that technology on commercially reasonable terms ~~, if at all~~. If we need to develop or acquire alternative manufacturing technology, our product development activities may be significantly delayed, and if we were unable to develop or acquire alternative manufacturing technology, it could have a material adverse effect on our business. In addition, we may not be able to prevent competitors from developing and commercializing competitive products to the extent our licenses to patents are non- exclusive or limited with respect to fields of use or territories. We anticipate that licenses to additional third- party technology will be required to advance our current development programs, as well as additional development programs we may initiate in the future. If these licenses are not available on commercially reasonable terms or at all, we may not be able to commercialize our current and future development programs, which will have a material adverse effect on our business and financial condition, results of operations and prospects. The patent protection and patent prosecution for some of our product candidates are dependent on third parties. While we normally seek to obtain the right to control the prosecution and maintenance of the patents relating to our product candidates, there may be times when the filing and prosecution activities for platform technology patents that relate to our product candidates are controlled by our licensors. For example, we do not have the right to prosecute and maintain the patent rights licensed to us under agreements with Regents of the University of California and Virovek, and our ability to have input into such filing and prosecution activities is limited. If these licensors or any of our future licensors fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We require all employees to sign proprietary information and invention assignment agreements, but they may fail to do so, or our agreements may be found invalid or unenforceable. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. 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 as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Third - party patent rights could delay or otherwise adversely affect our planned development and sale of product candidates of our programs. We are aware of patent rights held by third parties that could be construed to cover certain aspects of our product candidates. In addition, changes to our product candidates or their uses or manufacture may cause them to infringe patents held by third parties. A patent holder has the right to prevent others from making, using, importing or selling a drug that incorporates the patented compositions while the patent remains in force. While we believe that third - party patent rights will not affect our planned development, regulatory clearance, and eventual marketing, commercial production, and sale of our product candidates, there can be no assurance that this will be the case. In addition, the Drug Price Competition and Patent Term Restoration Act of 1984 (" Hatch- Waxman Act ") exemption provided by U. S. patent law permits uses of compounds and biologics in clinical trials and for other purposes reasonably related to obtaining FDA approval of drugs and biologics that will be sold only after patent expiration, so our use of our product candidates in those FDA-related activities does not infringe any patent holder' s rights. However, were a patent holder to assert its rights against us before expiration of such patent holder' s patent for activities unrelated to seeking FDA approval, the development and ultimate sale of our product candidates could be significantly delayed, and we could incur the expense of defending a patent infringement suit and potential liability for damages for periods prior to the patent' s expiration. We may not be able to obtain intellectual property rights or protect our intellectual property rights throughout the world. Filing, prosecuting, obtaining and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual

property rights in some countries outside the U. S. can be less extensive than those in the U. S. 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 U. S. Further, following Russia' s invasion of Ukraine in February 2022, the U. S. government has levied sanctions against Russia and Belarus, Russia has issued a decree that removes protections for some patent holders who are registered in unfriendly countries, including the U. S., and the USPTO has terminated its engagement with officials from intellectual property agencies in Russia, Belarus and Eurasia, so we are not currently maintaining certain intellectual property filings in these jurisdictions. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S., or from selling or importing products made using our inventions in and into the U. S. or other jurisdictions. 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 U. S. 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. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. 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 as patents 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 to us, if any, may not be commercially meaningful. For example, the complexity and uncertainty of European patent laws have also increased in recent years. In Europe, a new unitary patent system was introduced in 2023. Under the unitary patent system, European applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC- based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long- term effects of any potential changes. 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. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. 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 the U. S. 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. If we do not obtain patent term extensions for patents covering our product candidates, our business may be materially harmed. Patent terms may not be able to protect our competitive position for an adequate period of time with respect to our current or future technologies or product candidates. Patents have a limited lifespan. In the U. S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non- provisional filing date. As a result, our owned and in- licensed patent portfolio provides us with limited rights that may not last for a sufficient period of time to exclude others from commercializing product candidates similar or identical to ours. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. For example, given the large amount of time required for the research, 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Extensions of patent term may be available, but there is no guarantee that we would have patents eligible for extension, or that we would succeed in obtaining any particular extension — and no guarantee any such extension would confer a patent term for a sufficient period of time to exclude others from commercializing product candidates similar or identical to ours. If we are able to secure FDA marketing approval for one of our product candidates that is covered by an issued U. S. patent, that patent may be eligible for limited patent term restoration under the Hatch- Waxman Act. Depending upon the timing, duration and specifics of FDA marketing approval of product candidates, the Hatch- Waxman Act permits a patent restoration term of up to five years beyond the normal expiration of the patent, which is limited to the approved product or approved indication. In the U. S., patent term extension cannot extend the remaining term of a patent beyond 14 years from the date of product approval; only one patent may be extended; and extension is available for only those claims covering the approved drug, a method for using it, or a method for manufacturing it. Similar extensions of patent term are available in Europe and other jurisdictions. 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, and our business, financial conditions and results of operations may be materially and adversely affected. The interpretation by the regulatory authorities in the EU of applicable EU regulations governing data and market exclusivity may impact our entitlement to data and market exclusivity. The revisions to the orphan drug legislation in the EU and the EU rules governing Supplementary Protection Certificates that are currently being discussed may also impact our entitlement to this exclusivity. 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 administratively or in court. If we or any of our future development partners were to initiate or threaten legal proceedings against a third - party to enforce a patent directed at one of our product candidates, or one of our future product candidates, the accused infringer could claim that our patent is invalid and / or unenforceable in whole or in part. In patent litigation in the U. S., defendant counterclaims alleging invalidity and / or unenforceability are commonplace, as are claims seeking declaratory judgment of invalidity. 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 false or misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business. Interference proceedings provoked by third parties or brought by us or declared by the USPTO 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 harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or patent office 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 and development 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 or patent office 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. 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. Some intellectual property that we have in- licensed or may in- license may have been discovered through government funded programs and thus may be subject to federal regulations such as " march- in " rights, certain reporting requirements and a preference for U. S.- based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non- U. S. manufacturers. Intellectual property rights we have licensed, including certain rights related to our proprietary AAV. 7m8 capsid, were generated through the use of U. S. government funding and are therefore subject to certain federal regulations. As a result, the U. S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh- Dole Act of 1980 (" Bayh- Dole Act ") and implementing regulations. These U. S. government rights in certain inventions developed under a government- funded program include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right to require us or our licensors to grant exclusive, partially exclusive, or non- exclusive licenses to any of these inventions to a third - party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as " march- in rights "). The U. S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. These time limits have recently been changed by regulation, and may change in the future. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U. S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U. S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U. S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U. S. manufacturers may limit our ability, or that of our

sublicensees, to contract with non- U. S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U. S. government funding, the provisions of the Bayh- Dole Act may similarly apply. We may fail to comply with any of our obligations under existing 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. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding our rights to intellectual property licensed to us from a third - party, including but not limited to: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights; • our diligence obligations under the license agreement, what activities satisfy those diligence obligations, and to what extent those obligations are relieved or delayed by external factors beyond our control; • the ownership of inventions and know- how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators; • the scope and duration of our payment obligations; • our rights upon termination of such agreement; and • the scope and duration of exclusivity obligations of each party to the agreement. If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. 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 gene therapies that are similar to our product candidates but that are not covered by the claims of any patents that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • any patent applications that we have filed or may file in the future may not lead to issued patents; • any of the issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors; • any of the issued patents that we have filed or may file in the future may expire before or shortly after commercialization of the covered product; • our competitors might conduct research and development activities in countries where, or for products for which, 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 significantly harm our business, financial condition, results of operations and prospects. We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers. As is common in the biotechnology and pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of our employees and consultants were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that our company, 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. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact 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 team. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our registered or 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 registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could materially and adversely impact our business, financial condition, results of operations, or prospects. Risks Related to Commercialization of Our Product Candidates Any suspension of, or delays in the commencement or completion of, clinical trials for our product candidates could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects. We currently have one product candidate in clinical trials. Before we can initiate clinical trials for other product candidates in the U. S., we need to submit the results of nonclinical testing to the FDA, along with other information about the product candidate' s chemistry, manufacturing , and controls and our proposed clinical trial protocol, as part of an IND. Similar requirements may apply to conduct clinical trials outside the U. S. We may rely in part on nonclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. If these third parties do not provide timely data for our product candidates, it will delay our plans for our IND submissions or comparable foreign applications and clinical trials. If those third parties do not make this data available to us, we will likely have to develop

all necessary nonclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA or other regulatory authorities **outside the U. S.** may require us to conduct additional nonclinical testing for any of our product candidates before they allow us to initiate clinical trials under any IND or equivalent, or at any stage of clinical development of Ixo- vec or other new product candidates based on concerns that arise as the clinical program progresses or if significant manufacturing process changes are made to the program, which may lead to additional delays and increase the costs of our nonclinical development. Delays with any regulatory authority or agency may significantly affect our product development timeline. Delays in the commencement or completion of any clinical trials that we plan for our product candidates could significantly affect our product development costs. We do not know whether any clinical trials that we plan will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed or terminated for a number of reasons, including delays or terminations related to: • the FDA or other regulatory authorities outside the U. S. failing to grant permission to proceed or placing the clinical trial on hold; • patients failing to enroll or remain in our trial at the rate we expect; • patients choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials; • lack of adequate funding to continue the clinical trial; • patients experiencing severe or unexpected drug- related adverse effects; • a facility manufacturing any of our product candidates or any of their components being ordered by the FDA or other government or regulatory authorities outside the U. S., to temporarily or permanently shut down due to violations of GMP or other applicable requirements, or infections or cross- contaminations of product candidates in the manufacturing process, or in the manufacturing facilities in which our product candidates are made; • availability of non- investigational materials or supplies required for the clinical trials **; • availability of appropriate prophylaxis in geographies where we intend to conduct our Phase 3 clinical trials and to commercialize Ixo- vec, if approved** ; • any changes to our manufacturing process that may be necessary or desired; • availability of non- investigational materials or supplies required for manufacturing; • third- party clinical investigators losing the licenses, permits or resources necessary to perform our clinical trials, lacking the ability or resources to appropriately handle our product candidates, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practice or regulatory requirements, or other third parties not performing data collection, sample testing or analysis in a timely and accurate manner; • inspections of clinical trial sites by the FDA or other regulatory authorities outside the U. S., or the finding of regulatory violations by the FDA or other regulatory authorities outside the U. S., or an IRB or Ethics Committee that requires us to undertake corrective action resulting in suspension or termination of one or more clinical sites or the imposition of a clinical hold on the IND or foreign equivalent or that prohibits us from using some or all of the data in support of our marketing applications; • third- party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities outside the U. S. for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or • one or more IRBs or Ethics Committees refusing to approve, suspending or terminating the trial at a clinical site, precluding enrollment of additional patients, or withdrawing its approval of the trial. Product development costs will increase if we have delays in testing or approval of any of our product candidates, or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to competent authorities, IRBs or Ethics Committees for review and approval, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in the completion of our clinical trials, or if we, the FDA or other regulatory authorities outside the U. S., the IRB or Ethics Committee, other reviewing entities, or any of our clinical trial sites, suspend or terminate any of our clinical trials, the commercial prospects for our product candidate may be harmed and our ability to generate product revenue may be delayed. In addition, many of the factors that cause, or lead to, the termination or suspension of, or a delay in the commencement or completion of, clinical trials, may also ultimately lead to the denial of regulatory approval of a product candidate. If we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Further, if one or more clinical trials are delayed or terminated, our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. We have amended our clinical trial protocols and from time to time may further amend our clinical trial protocols based on a variety of factors, and these changes may have unanticipated consequences on our clinical trial outcomes. Final marketing approval for our product candidates by the FDA or other regulatory authorities outside the U. S. for commercial use may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenue. Even if we are able to successfully complete our clinical trials and submit a BLA, and / or an MAA, we cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates, and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize our product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory authorities will complete their review processes in a timely manner or that we will obtain regulatory approval for our product candidates. **For example, difluprednate eye drops are not approved or commercially available in certain geographies where we intend or may choose to seek regulatory approval for Ixo- vec, and we cannot assure you that the appropriate prophylaxis will be available in such jurisdictions to enable us to obtain regulatory approval to commercialize Ixo- vec.** In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in policies from the FDA or other regulatory authorities outside the U. S. during the period of product development, clinical trials and FDA' s or comparable foreign regulatory authorities' regulatory review. If marketing approval for any product candidate is delayed, limited or denied, our ability to market the product candidate ~~,~~ and our ability to generate product sales, would be adversely affected **. Disruptions at the FDA or other agencies may also slow the time necessary for new drugs to be reviewed and / or approved by necessary**

government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government shut down several times and certain regulatory agencies, such as the FDA, furloughed critical employees and ceased critical activities. More recently, such agencies, including the FDA, have conducted layoffs and may, from time to time, conduct additional layoffs. If a prolonged government shutdown or significant layoffs occur, it could significantly impact the ability of the FDA and applicable foreign authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business . Even if we receive regulatory approval, we still may not be able to successfully commercialize any of our product candidates, and the revenue that we generate from product sales, if any, could be limited. Even if one or more of our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payers or the medical community. Coverage and reimbursement of our product candidates by third- party payers, including government payers, is also generally necessary for commercial success. The degree of market acceptance of our product candidates will depend on a number of factors, including: • demonstration of clinical efficacy, including duration of efficacy, and safety compared to competitive products, some of which are more established than our product candidates **; • availability and market acceptance of an appropriate prophylaxis regimen in geographies where we intend to commercialize Ixo- vec, if approved** ; • the limitation of our targeted patient population and other limitations or warnings contained in any labeling approved for our product candidates by the FDA or other applicable regulatory authorities outside the U. S., including the possible inclusion of a " black box warning " from the FDA or other applicable regulatory authorities outside the U. S., alerting healthcare providers to potential serious side effects associated with using a product or the imposition of a Risk Evaluation and Mitigation Strategy (" REMS ") or comparable foreign strategies; • acceptance of new therapeutic options by healthcare providers and their patients; • the prevalence and severity of any adverse effects; • new procedures or methods of treatment that may be more effective in treating or may reduce the incidence of wet AMD, or other conditions that our product candidates are intended to treat; • pricing and cost- effectiveness; • the effectiveness of our or any future collaborators' sales and marketing strategies; • our ability to obtain and maintain sufficient third- party coverage and reimbursement from government health care programs, including Medicare and Medicaid or foreign equivalents, private health insurers and other third- party payers; and • the willingness of patients to pay out- of- pocket in the absence of third- party coverage and reimbursement. If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payers or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third- party payers on the benefits of such a product candidate may require significant resources and may never be successful. In addition, our ability to successfully commercialize any of our product candidates will depend on our ability to manufacture our products, differentiate our products from competing products, and defend and enforce our intellectual property rights relating to our products. If our competitors develop treatments for the target indications of our product candidates that are approved, marketed more successfully, or demonstrated to be safer or more effective or easier to administer than our product candidates, our commercial opportunity will be reduced or eliminated. We operate in highly competitive segments of the biopharmaceutical markets. We face competition from many different sources, including larger and better- funded pharmaceutical, specialty pharmaceutical, biotechnology, and gene therapy companies, as well as from academic institutions, government agencies and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies as well as with new treatments that may be introduced by our competitors. There are a variety of drug candidates and gene therapies in development or being commercialized by our competitors for the indications that we intend to test. Many of our competitors have significantly greater financial, product candidate development, manufacturing, and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. In addition, universities and private and public research institutes may be active in our target disease areas, and some could be in direct competition with us. We also may compete with these organizations to recruit management, scientists, and clinical development personnel. We will also face competition from these third parties in establishing clinical trial sites, registering patients for clinical trials, and in identifying and in- licensing new product candidates. For example, ~~REGENXBIO~~ **4D Molecular Therapeutics** is developing ~~RGX~~ **4D** - ~~314~~ **150** , an AAV- based gene therapy delivering ~~a gene~~ **two transgenes and** encoding a therapeutic antibody fragment similar to ~~ranibizumab~~ **aflibercept** (**Eylea** ~~LUCENTIS ®~~) for the treatment of wet AMD and diabetic ~~retinopathy~~ **macular edema** , which competes for the same patients, study site resources ~~,~~ and personnel as Ixo- vec. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. New developments, including the development of other biotechnology and gene therapy technologies and methods of treating disease, occur in the pharmaceutical, biotechnology and gene therapy industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. Competition in drug development is intense. In addition, we believe that duration of efficacy is an important consideration by physicians and patients when choosing a therapy. However, we do not know and may not know prior to any potential approval the duration of efficacy of our product candidates. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available. Even if we obtain regulatory approval for our product candidates, the availability and price of our competitors' products could limit the demand, and the price we are able to charge ~~,~~ for our product candidates. For example, LUCENTIS (and biosimilars thereto), EYLEA **(and any biosimilars thereto)** and VABYSMO **(and any biosimilars thereto)** are currently available **or will become available** in the U. S. and the EU for treatment of wet AMD. We ~~will~~ **may** not achieve our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances. Our inability to compete with existing or subsequently introduced drug products or other therapies would have a material adverse impact on our business, prospects, financial condition and results of operations. Our potential

competitors in these diseases may be developing novel therapies that may be safer or more effective or easier to administer than our product candidates. For example, if we continue clinical development of, and seek to commercialize, Ixo- vec for the treatment of wet AMD, it will compete with a variety of therapies currently marketed and in development for wet AMD, using therapeutic modalities such as biologics, small molecules, long- acting delivery devices and gene therapy. In the United States, most patients receive off- label bevacizumab, including as a first- line treatment. Many patients go on to receive Eylea, Eylea HD ~~and~~ **or** Vabysmo ® (faricimab **- svoa**). We know of a ~~significant~~ number of **additional** product candidates in development or ~~recently~~ approved for chronic retinal conditions that respond to anti- VEGF therapy, including wet AMD: • biosimilar anti- VEGFs ~~(e. g., FYB201)~~ ; • bispecific / combination / add- on therapy for efficacy or durability improvement ~~(e. g., Vabysmo and OPT- 302); • next- generation anti- VEGF for durability improvement (e. g., Eylea HD)~~ ; • long- acting delivery device ~~/ gene therapy~~ **and tyrosine kinase inhibitor implants** to lower treatment frequency **; • gene therapy to lower treatment frequency** (e. g., 4D- 150, RGX- 314 and **offer the potential for lifelong injection freedom** ~~Susvimo, which is Roche' s Port Delivery System with ranibizumab)~~ ; and • other molecules that inhibit neovascularization in wet AMD ~~(e. g., tyrosine kinase inhibitors such as OKT- TKI and EYP- 1901)~~ . There are several other companies in the U. S. or Europe with marketed products or products in development for the treatment of chronic retinal conditions that respond to anti- VEGF therapy, including wet AMD. These companies include 4D Molecular Therapeutics, AbbVie, Bayer, Clearside Biomedical, EyePoint Pharmaceuticals, Kodiak Sciences, Novartis, Ocular Therapeutix, Opthea, Outlook Therapeutics, Regeneron, REGENXBIO and Roche. Even if we obtain marketing approval for any of our product candidates, they could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved. Even if regulatory approval is obtained, the FDA or comparable foreign regulatory authorities may still impose significant restrictions on a product' s indicated uses, marketing or distribution or impose ongoing requirements for potentially costly and time- consuming post- approval studies, post- market surveillance or clinical trials. Following approval, if at all, of any of our product candidates, such candidate will also be subject to ongoing FDA and comparable foreign requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post- market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities outside the U. S. for compliance with GMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents. If we or a regulatory authority 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, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing. If we or the manufacturing facilities for any product candidate that may receive regulatory approval fail to comply with applicable regulatory requirements, a regulatory authority may: • issue warning letters or untitled letters; • seek an injunction or impose civil or criminal penalties or monetary fines; • suspend, vary or withdraw regulatory approval; • suspend any ongoing clinical trials; • refuse to approve pending applications or supplements or applications filed by us; • institute import holds; • suspend or impose restrictions on operations, including costly new manufacturing requirements; or • seize or detain products, refuse to permit the import or export of product or request us to initiate a product recall. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue. The FDA has the authority to require a REMS plan as part of a BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe- use criteria and requiring treated patients to enroll in a registry. Similar restrictions may be imposed by foreign regulatory authorities outside the U. S. In addition, if any of our product candidates is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and ongoing regulatory review. The FDA and other regulatory authorities outside the U. S. strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the competent regulatory authority as reflected in the product' s approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off- label uses, we may become subject to significant liability. The FDA and regulatory and enforcement authorities outside the U. S. actively enforce the laws and regulations prohibiting the promotion of off- label uses, and a company that is found to have improperly promoted off- label uses may be subject to significant sanctions. The U. S. federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or be subject to permanent injunctions under which specified promotional conduct is changed or curtailed. Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably. Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third- party payers for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third- party payers, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third- party payer may depend upon a number of factors including the third- party payer' s determination that use of a product candidate is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; and • cost- effective. Obtaining coverage and reimbursement approval for a product candidate from a government or other third- party payer is a time- consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of the applicable product candidate to the payer. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. While there is no

uniform coverage and reimbursement policy among payers in the U. S., private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, reimbursement amounts may reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved. A number of cell and gene therapy products recently have been approved by the FDA. Although the U. S. Centers for Medicare & Medicaid Services (" CMS ") approved its first method of coverage and reimbursement for gene therapy products, the methodology has been subject to challenge by members of Congress. CMS' s decision as to coverage and reimbursement for one product does not mean that all similar products will be eligible for analogous coverage and reimbursement. As there is no uniform policy for coverage and reimbursement amongst third- party payers in the U. S., even if CMS approves coverage and reimbursement for any of our product candidates, it is unclear what affect, if any, such a decision will have on our ability to obtain and maintain coverage and adequate reimbursement from other private payers. Third- party payers are increasingly challenging the price and examining the medical necessity and cost- effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost- effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third- party payers do not consider a product to be cost- effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans. or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. **Further, coverage policies and third- party payer reimbursement rates may change at any time. Therefore, even if favorable coverage and reimbursement status is attained for one or more products for which we receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.** The U. S. government, state legislatures, and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government- paid health care costs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products for branded prescription drugs. By way of example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the " Affordable Care Act "), was enacted with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care organizations and established annual fees and taxes on manufacturers of certain prescription drugs. Certain provisions of the Affordable Care Act have been subject to **amendments and** executive, Congressional, and judicial challenges as well as efforts to repeal, replace, or otherwise modify them or alter their interpretation and implementation. For example, ~~the TCJA included a provision that repealed, effective January 1, 2019, the tax- based shared responsibility payment imposed by the Affordable Care Act~~ on ~~certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the " individual mandate. " Additionally, on June 17, 2021 the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Further, prior to the U. S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act 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, policies that undermine protections for people with pre- existing conditions, demonstrations and waivers under Medicaid and the Affordable Care Act that may reduce coverage or undermine the programs thereunder, including work requirements, and policies that make it more difficult to access health benefits through Medicaid or the Affordable Care Act. On~~ August 16, 2022, ~~President Biden signed~~ the Inflation Reduction Act of 2022 (the " Inflation Reduction Act ") **was signed** into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The Inflation Reduction Act also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost and through a newly established manufacturer discount program. Additional legislative changes, regulatory changes, and judicial challenges related to the Affordable Care Act remain possible. Any such changes could affect the number of individuals with health coverage. It is possible that the Affordable Care Act, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to successfully commercialize our product candidates, if approved. Outside the United States, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. The EU provides options for EU Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product, it may refuse to reimburse a product at the price set by the manufacturer or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Many EU Member States also periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost- effectiveness of our products to other available therapies. This Health Technology Assessment (" HTA ") of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those

representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. Legislators, policymakers and healthcare insurance funds in the EU and the United Kingdom may continue to propose and implement cost- containing measures to keep healthcare costs down. These measures could include limitations on the prices we would be able to charge for product candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third- party ~~payors~~ **payers** . Further, an increasing number of EU and other foreign countries use prices for medicinal products established in other countries as " reference prices " to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere. Healthcare and other reform legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and, if approved, may affect the prices we may obtain. Legislative changes have also been proposed and adopted in the U. S. since the Affordable Care Act was enacted. For example, on August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $ 1. 2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation' s automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of, on average, 2 % per fiscal year, which went into effect on April 1, 2013 and due to subsequent legislative changes to the statute, will stay in effect until 2032 unless additional congressional action is taken. Further, ~~Congress is considering~~ **there may be** additional health reform measures **, particularly in light of recent U. S. presidential and congressional elections** . These cost reduction initiatives could decrease the coverage and reimbursement that we receive for any approved products and could seriously harm our business. ~~The Biden administration expressed its intent to pursue certain policy initiatives to reduce drug prices.~~ For example ~~, in July 2021, the Biden administration released an executive order, " Promoting Competition in the American Economy, " with multiple provisions aimed at prescription drugs. In response to Biden' s executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. Further~~ , the Inflation Reduction Act, among other things, (1) directs **the U. S. Department of Health and Human Services (" HHS ")** to negotiate the price of certain single- source ~~drugs and~~ biologics **that have been on the market for at least 11 years** covered under Medicare **(the " Medicare Drug Price Negotiation Program ")** and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions began to take effect beginning fiscal year 2023. On August ~~29~~ **15** , ~~2023~~ **2024** , HHS announced the ~~list~~ **agreed- upon reimbursement price** of the first ten drugs that **were** ~~will be~~ subject to price negotiations, although the Medicare ~~drug~~ **Drug** ~~price~~ **Price** ~~negotiation~~ **Negotiation** ~~program~~ **Program** is currently subject to legal challenges **. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more products covered under Part B and Part D will become subject to the Medicare Drug Price Negotiation Program** . The Inflation Reduction Act permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. ~~It is unclear how the Inflation Reduction Act will be implemented but is likely to have a significant impact on the pharmaceutical industry. In response to the Biden administration' s October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.~~ Further, on December 7, 2023, ~~the Biden administration announced~~ an initiative to control the price of prescription drugs through the use of march- in rights under the Bayh- Dole Act **was announced** . On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework. We expect that additional healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our product candidates, if approved, or additional pricing pressures. The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of health care may adversely affect: • the demand for any product candidates for which we may obtain regulatory approval; • our ability to set a price that we believe is fair for our product candidates; • our ability to generate revenue and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital. In December 2021, Regulation No 2021 / 2282 on HTA amending Directive 2011 / 24 / EU, was adopted in the EU. This Regulation, which entered into force in January 2022 and ~~will~~ **began to** apply **on** ~~as of~~ January **12,** 2025 **, through a phased implementation** , is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. The Regulation foresees a three- year transitional period and ~~will permit~~ **permits** EU Member States to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health

technologies, and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU Member States for product candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected. In light of the fact that the United Kingdom has left the EU, Regulation No 2021 / 2282 on HTA will not apply in the United Kingdom. However, the UK MHRA is working with UK HTA bodies and other national organizations, such as the Scottish Medicines Consortium (" SMC "), the National Institute for Health and Care Excellence (" NICE "), and the All- Wales Medicines Strategy Group, to introduce new pathways supporting innovative approaches to the safe, timely and efficient development of medicinal products. If the market for Ixo- vec, if approved, in the treatment of wet AMD or any other indication we seek to treat is smaller than we believe it is, or if our product candidate is approved with limitations that reduce the market size, or if this occurs for any of our other product candidates, our future revenue may be adversely affected, and our business may suffer. We are advancing the development of Ixo- vec for the treatment of wet AMD, which is a leading cause of blindness in patients over 65 years of age. If the size of the market for wet AMD or any other indication we seek to treat is smaller than we anticipate, we may not be able to achieve profitability and growth. Our projections of the number of people who have wet AMD and other indications, as well as the subset of people with the disease who have the potential to benefit from treatment with Ixo- vec or other future product candidates, are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations and market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in **its** early stages. We cannot accurately predict the number of patients for whom treatment for wet AMD using Ixo- vec or any of our other product candidates might be possible or whether the FDA or other regulatory authorities **outside the U. S.** may approve indications for Ixo- vec or any of our other product candidates that are more limited than we expect due to efficacy or safety concerns. For example, some patients have neutralizing antibodies at titer levels that may prevent them from benefiting from Ixo- vec. If this patient population is larger than we estimate, the market for Ixo- vec may be smaller than we anticipate, and our future revenue may be adversely affected. In addition, we expect prophylactic corticosteroid treatment will be required to manage inflammation associated with treatment with Ixo- vec, and certain patients cannot be treated with prophylactic corticosteroids. If this proportion of the patient population is larger than we estimate, the market for Ixo- vec may be smaller than we anticipate. Additionally, the potentially addressable patient population may be limited or may not be amenable to treatment with our product candidates for other reasons, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our product candidates, if approved, may be delayed and the credibility of our management team may be adversely affected and, as a result, our stock price may decline. From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of, or the availability of data from, scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones will be based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our management team may be adversely affected and, as a result, our stock price may decline. Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates. Our product candidates are designed to provide potential therapeutic benefit after a single administration and, therefore, the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e. g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our product candidates. We may not be successful in establishing and maintaining development **, commercialization** or other strategic collaborations, which could adversely affect our ability to develop and commercialize product candidates and receive milestone and / or royalty payments. We have entered into development or other strategic collaborations with biotechnology and pharmaceutical companies in the past **,** and may ~~do so again~~ in the future **enter into additional development, commercialization or other strategic collaborations** . Research activities under our collaboration agreements may be subject to mutually agreed- on research plans and budgets, and if we and our strategic partners are unable to agree on the research plan or research budget in a timely fashion or at all, performance of research activities will be delayed. In addition, some of our strategic partners may terminate any agreements they enter into with us or allow such agreements to expire by their terms. If we fail to maintain our current or future strategic collaborations, we may not realize milestone and royalty payments or other revenues under the collaboration agreements. Governments may impose price controls, which may adversely affect our future profitability. We intend to seek approval to market our product candidates in both the U. S. and in foreign jurisdictions. If we obtain approval in one or more jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product candidates. In some countries, including Member States of the European Economic Area (" EEA "), the pricing of prescription pharmaceuticals is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. There can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and

reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low- priced and high- priced countries, can further reduce prices. Publication of discounts by third- party payers or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability. We may form strategic alliances in the future, and we may not realize the benefits of such alliances. We may form strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of our product candidates. These relationships or those like them may require us to incur non- recurring and other charges, increase our near- and long- term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time- consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because third parties may view the risk of failure in future clinical trials as too significant, or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such development partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are disappointing. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market. We have no sales, marketing, distribution, or market access and reimbursement capabilities, and we would have to **establish a partnering arrangement and / or** invest significant resources to develop these capabilities. We have no internal sales, marketing, distribution, or market access and reimbursement capabilities. If any of our product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We would have to **establish a partnering arrangement for commercialization and / or** invest significant amounts of financial and management resources to develop internal sales, marketing, distribution, or market access and reimbursement capabilities, some of which will be committed prior to any confirmation that any of our product candidates will be approved, if at all. We may not be able to hire consultants or external service providers to assist us in sales, marketing, distribution, or market access and reimbursement functions on acceptable financial terms or at all. Even if we determine to perform sales, marketing, distribution, or market access and reimbursement functions ourselves, we could face a number of additional related risks, including: • we may not be able to attract and build an effective marketing department, sales force, or distribution capabilities; • the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by any product candidates that we may develop, in- license or acquire; and • our direct sales and marketing efforts may not be successful. Risks Related to Our Business Operations Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing symptomatic treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. Trials using early versions of retroviral vectors, which integrate into, and thereby alter, the host cell' s DNA, have led to several well- publicized adverse events. Although none of our current product candidates utilize retroviruses and we believe AAVs used in our product candidates have low- integrating potential and are not known to cause disease in humans, our product candidates do use a viral vector delivery system. The risk of serious adverse events, such as the dose- limiting toxicity at the 6E11 dose tested in our INFINITY trial, remains a concern for gene therapy and we cannot assure that it will not occur in any of our current or future clinical trials. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Adverse events in trials or studies conducted by us or other parties, in particular involving the same or similar AAV serotypes to the ones we are using, even if not ultimately attributable to our product candidates or to an AAV serotype that we employ, and resulting publicity, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. Similarly, our lead product candidate, Ixo- vec, ~~expresses~~ **leads to expression of a codon- optimized version of** the aflibercept protein, which is also the active component in ~~EYLEA~~ **Eylea** . If safety or efficacy issues occur relating to ~~EYLEA~~ **Eylea** , even if not ultimately attributable to aflibercept, this may negatively impact our product candidate. If any such adverse events or issues occur, development and commercialization of our product candidates or advancement of any potential clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations. We are dependent on the services of our key executives and clinical and scientific staff, and if we are not able to retain these members of our management or recruit additional management, clinical and scientific personnel, our business will suffer. We are dependent on the principal members of our management, clinical and scientific staff. The loss of service of any of our management or clinical or scientific staff could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management, and to attract, on acceptable terms, additional qualified personnel necessary for the

continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. ~~We~~ **Previously, we** have had significant changes in our executive management team, and from time to time, may experience additional changes in our executive management team resulting from the hiring or departure of executives. While we seek to manage these transitions carefully, these and any other such changes may result in a loss of institutional knowledge and cause disruptions to our business. We may not be able to attract or retain qualified management, scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. ~~Our~~ **At various times in recent years, our** industry has experienced a high rate of turnover of management and scientific personnel ~~in recent years~~. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy. Additionally, we do not currently maintain " key person " life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals. We may encounter difficulties in managing our growth and expanding our operations successfully. In the future, we will need to grow our organization, or certain functions within our organization, substantially **and potentially establish partnering agreements** to continue development and pursue the potential commercialization of our product candidates, as well as function as a public company. As we seek to advance our product candidates, we may need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain or otherwise manage additional internal capabilities. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate any additional management, clinical and regulatory, financial, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish them could prevent us from successfully growing our company. If our information technology systems or those third parties ~~upon which~~ **with whom** we ~~rely~~ **work**, or our data, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; material disruption of our product development programs; and other adverse consequences. In the ordinary course of our business, we and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work**, process, collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit and share (collectively, process) proprietary, confidential, and sensitive data, including personal data (such as health- related data), intellectual property and trade secrets (collectively, sensitive information). Cyber- attacks, malicious internet- based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties ~~upon which~~ **with whom** we ~~rely~~ **work**. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer " hackers, " threat actors, " hacktivists, " organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation- state- supported actors. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation- state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we **,** and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work,** may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. We and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** are subject to a variety of evolving threats, including but not limited to social- engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of- service attacks, credential stuffing attacks, credential harvesting, personnel misconduct or error, ransomware attacks, supply- chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fires, floods, attacks enhanced or facilitated by AI, and other similar threats. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, disruptions of clinical trials, ability to provide our services, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Remote work has ~~become more common and has~~ increased risks to our information technology systems and data, as more of our employees utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit and in public locations. ~~Additionally, future~~ **Future** or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. We rely on third **parties** ~~party service providers and technologies~~ to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, CROs, CMOs, collaborators, cloud- based infrastructure, data center facilities, encryption and authentication technology, employee email, content delivery to customers, and other functions. Our ability to monitor these third

parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If ~~our~~ **the** third ~~- party service providers~~ **parties with whom we work** experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if ~~our~~ **the** third ~~- party service providers~~ **parties with whom we work** fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or ~~our~~ **that of the** third ~~- party partners~~ **parties** ~~' supply chains~~ **with whom we work** have not been compromised ~~. While we may be entitled to damages if our third- party service providers fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our services. We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures, industry- standard or reasonable security measures to protect our information technology systems and confidential, sensitive, or proprietary information. For example, the loss of clinical trial information from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the information~~ . While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate, and remediate vulnerabilities in our information systems (such as our hardware and / or software, including that of third parties ~~upon which~~ **with whom** we ~~rely~~ **work**). We may not, however, detect and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in **developing and** deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in **the** unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties ~~upon~~ **with** whom we ~~rely~~ **work. For example, in December 2024, we were the target of nine unsuccessful phishing attempts and expect such attempts will continue in the future and we cannot guarantee that our employees will not succumb to, or that our security measures will adequately detect or prevent, such phishing attacks** . A security incident or other interruption could disrupt our ability (and that of third parties ~~upon~~ **with** whom we ~~rely~~ **work**) to provide our services. We ~~may~~ expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations ~~may~~ require us to implement and maintain specific security measures ~~or~~ **,** industry- standard or reasonable security measures to protect our information technology systems and sensitive information. **For example, the loss of clinical trial information from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the information.** Applicable data privacy and security obligations may require us **, or we may voluntarily choose,** to notify relevant stakeholders, **including partners, affected individuals, regulators, and investors of security incidents, or to take other actions,** such as **providing credit monitoring** ~~governmental authorities, partners,~~ and **identity theft protection services** ~~affected individuals, of security incidents~~ . Such disclosures ~~may involve inconsistent requirements~~ and ~~are~~ **related actions can be** costly, and the disclosures or the failure to comply with such **applicable** requirements could lead to adverse consequences. If we (or a third **-** party ~~upon~~ **with** whom we ~~rely~~ **work**) experience a security incident or are perceived to have experienced a security incident, we may experience **material** adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and / or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; diversion of management attention; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant **material** consequences may prevent or cause customers to stop using our ~~platform / products /~~ services, deter new customers from using our services, and negatively impact our ability to grow and operate our business. A security incident could also disrupt our operations, including our ability to conduct research and development activities, process and prepare company financial information, manage various general and administrative aspects of our business, delay or impede the development of our products, and damage our reputation, any of which could adversely affect our business. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security incident were to result in a loss of, or damage to, our ~~data~~ **sensitive information** or applications, or inappropriate disclosure of **such sensitive** ~~confidential or proprietary~~ information, we could incur liability **,** and the further development and commercialization of our product candidates could be delayed. In addition, there can be no assurance that we will promptly detect any such disruption or security incident, if at all. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our ~~data~~ privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our data privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims. In addition to experiencing a security incident, third parties may gather, collect, or infer ~~confidential,~~ sensitive

~~, or proprietary~~ information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position **. Additionally, our sensitive information could be leaked, disclosed, or revealed as a result of or in connection with employees', contractors' or vendors' use of generative artificial intelligence (" AI ") technologies**. If we fail to comply with applicable state and federal healthcare laws and regulations, we may be subject to civil or criminal penalties and / or exclusion from federal and / or state healthcare programs, or foreign equivalents. In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws restrict certain practices, including research and marketing, in the pharmaceutical industry, and foreign equivalents. These laws include anti- kickback, false claims, and healthcare professional payment transparency laws and regulations. Because of the breadth of these laws and the narrowness of their exceptions and safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws. The federal Anti- Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward the purchasing, leasing, ordering, arranging for, or recommending the purchase, lease or order of any healthcare item or service for which payment may be made, in whole or in part, under Medicare, Medicaid or other federally financed healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced- price items and services. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formula managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices may be subject to scrutiny if they do not qualify for an exception or safe harbor. Liability may be established under the federal Anti- Kickback Statute without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute **,** constitutes a false or fraudulent claim for purposes of the False Claims Act. Many states have similar laws that apply to their state health care programs as well as private payers. The federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA ") imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third- party payers; knowingly and willfully embezzling or stealing from a healthcare benefit program; willfully obstructing a criminal investigation of a healthcare offense; and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. **HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (" HITECH ") and their respective implementing regulations, which impose obligations on covered health care providers, health plans, and health care clearinghouses, as well as their business associates that create, receive, maintain, or transmit individually identifiable health information for or on behalf of a covered entity and their subcontractors that use, disclose, access, or otherwise process protected health information, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.** The federal civil False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to be made or used, a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in significant monetary penalties and treble damages. Pharmaceutical and other healthcare companies have faced enforcement actions under the federal civil False Claims Act for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product and for allegedly causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non- reimbursable, uses. In addition, a claim can be deemed to be false due to failure to comply with legal or regulatory requirements material to the government' s payment decision. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false claim or statement. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes. In addition, there **is an** ~~has been a recent trend of increased~~ **increase in** federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposed new reporting requirements on drug manufacturers, under the federal Physician Payments Sunshine Act, for payments and other transfers of value made by them to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain other healthcare professionals (such as a physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in significant civil monetary penalties, for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states and localities also mandate implementation of commercial compliance programs, restrict the ability of manufacturers to offer co- pay support to patients for certain prescription drugs, impose restrictions on drug manufacturer marketing practices, require the tracking and reporting of gifts, compensation and other remuneration to physicians and / or require the registration of pharmaceutical sales representatives. Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti- bribery laws of European countries, national sunshine rules, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. We will need to build and maintain a robust compliance program with different compliance and / or reporting requirements. We cannot ensure that our

compliance controls, policies, and procedures will be sufficient to protect against acts of our employees, vendors, or other third parties that may violate such laws. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, imprisonment, and additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. 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 if we commercialize our product candidates. For example, we may be sued if our product candidates allegedly caused or cause injury or are found to be otherwise unsuitable during product 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 candidate, negligence, strict liability, and 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 limit or cease the commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for our products or product candidates; • injury to our reputation; • withdrawal of clinical trial participants; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to trial participants or patients; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • the inability to commercialize our product candidates; and • a decline in our stock price. We currently hold $ 10 million in product liability insurance, which may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our product candidates. Although we plan to maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also 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. We **and the third parties with whom we work** are subject to stringent and ~~changing~~ **evolving** U. S. and foreign laws, regulations, rules, contractual obligations **, industry standards** , policies, and other obligations related to data privacy and security. Our **(or the third parties with whom we work)** actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation **(including class claims) and mass arbitration demands** , fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, interruption of our clinical trials, and other adverse business consequences. In the ordinary course of business, we process sensitive information, including personal data, business data, trade secrets, intellectual property, and data we collect about trial participants in connection with clinical trials. Our data processing activities subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security, including information that we collect or will collect about clinical trial subjects and healthcare providers in connection with clinical trials. In the U. S., federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e. g., Section 5 of the Federal Trade Commission Act), and other similar laws (e. g., wiretapping laws). For example, HIPAA, as amended by the ~~Health Information Technology for Economic and Clinical Health Act (~~" HITECH ~~")~~, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable protected health information. We ~~may~~ obtain health information from third parties, such as research institutions, that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA other than with respect to providing certain employee benefits, we could potentially be subject to penalties if we, our affiliates, or our agents obtain, use, or disclose individually identifiable health information maintained by a HIPAA- covered entity in a manner that is not authorized or permitted by HIPAA. ~~In the past few years, numerous~~ **Numerous** U. S. states ~~— including California, Virginia, Colorado, Connecticut, and Utah —~~ have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt- out of certain data processing activities, such as targeted advertising, profiling, and automated decision- making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018 ~~, as amended by the California Privacy Rights Act of 2020~~ (**the** ~~" CPRA "), (collectively,~~" CCPA ") applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA provides for fines ~~of up to $ 7, 500 per intentional violation~~ and allows private litigants affected by certain data breaches to recover significant statutory damages. **The** ~~Although the~~ CCPA **and other comprehensive U. S. privacy laws** ~~exempts~~ **exempt** some data processed in the context of clinical trials, **but** ~~the~~ **these** ~~CCPA~~ **developments may further complicate compliance efforts, and** ~~increases~~ **increase legal risk and** compliance costs **for us,** and ~~potential liability~~ **the third parties** with **whom** ~~respect to other personal data~~ we **work** ~~maintain about California residents~~.

Similar laws are being considered in several other states, as well as at the federal and local levels, and we expect more states to pass similar laws in the future ~~. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely~~ . Outside the U. S., an increasing number of laws, regulations, and industry standards govern data privacy and security. For example, the European Union' s General Data Protection Regulation 2016 / 679 (" EU GDPR "), the United Kingdom' s GDPR (" UK **GDPR ", and, together with the EU GDPR, the "** GDPR "), Brazil' s General Data Protection Law (Lei Geral de Proteção de Dados Pessoais, or " LGPD ") (Law No. 13, 709 / 2018), and China' s Personal Information Protection Law (" PIPL ") impose strict requirements for processing personal data. For example, under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros under the EU GDPR, 17. 5 million pounds sterling under the UK GDPR or, in each case, 4 % of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized by law to represent their interests. ~~EU member states are also able to legislate separately on health and genetic information, and we must comply with these local laws where we operate.~~ In the ordinary course of business, we ~~may~~ transfer personal data from Europe and other jurisdictions to the U. S. or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the EEA and the UK have significantly restricted the transfer of personal data to the U. S. and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt **or have already adopted** similarly stringent ~~interpretations of their~~ data localization and cross- border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the U. S. in compliance with law, such as the EEA' s standard contractual clauses, the UK' s International Data Transfer Agreement / Addendum, and the EU- U. S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U. S.- based organizations who self- certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the U. S. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the U. S., or if the requirements for a legally- compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the U. S., are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the GDPR' s cross- border data transfer limitations. In addition to data privacy and security laws, we are contractually subject to industry standards adopted by industry groups and, we are, or may become subject to such obligations in the future. We are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. **For example, certain privacy laws, such as the GDPR and the CCPA, require our customers to impose specific contractual restrictions on their service providers. Our employees and contractors use generative AI technologies to perform work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance, costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.** Obligations related to data privacy and security (and consumers' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources, which may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. **In addition, these** ~~We may also be bound by contractual~~ obligations ~~related to data privacy and security, and our efforts to comply with such obligations~~ may ~~not be successful~~ **require us to change our business model** . We publish privacy policies, marketing materials **, presentations,** and other statements regarding data privacy and security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties ~~on~~ **with** whom we ~~rely~~ **work** may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties ~~on which~~ **with whom** we ~~rely~~ **work** fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e. g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class- action claims) and mass arbitration demands; additional reporting requirements and / or oversight; bans **or restrictions** on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. In particular, plaintiffs have become increasingly more active in bringing privacy- related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials) **; interruptions or stoppages of data collection needed to train our algorithms** ; inability to process personal data or to operate

in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations. We are subject to certain U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations (collectively, " Trade Laws "). We can face serious consequences for violations. Among other matters, Trade Laws prohibit companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, provide, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else or anything of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax assessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We also expect our non- U. S. activities to increase in time. We engage third parties for clinical trials and / or obtain necessary permits, licenses, registrations, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. We and our development partners, third- party manufacturers and suppliers use biological materials and use or may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly. We and our development partners, third- party manufacturers and suppliers use or may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third- party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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. We and any of our ~~future~~ development partners will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business. If we and any of our ~~future~~ development partners are successful in commercializing our products, the FDA and foreign regulatory authorities will require that we and any of our future development partners report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our future development partners may fail to report adverse events we become aware of within the prescribed timeframe. We and any of our future development partners may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our product candidates. If we and any of our future development partners fail to comply with our or their reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of the product and delay in approval or clearance of other products. Our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with our code of conduct or regulatory standards and requirements. We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in misconduct including code of conduct violations, fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct, or disclosure of unauthorized activities to us that violates: (1) FDA or comparable foreign regulations, including those laws requiring the reporting of true, complete and accurate information to regulatory authorities, (2) manufacturing standards, (3) federal, state and foreign health care fraud and abuse laws and regulations or (4) laws that require the reporting of financial information or data accurately. Specifically, sales, marketing, and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter 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 or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs or comparable foreign programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Our ability to use net operating loss carryforwards and other tax attributes may be limited by the Code. We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire, except as described below. Under the Tax Cuts and Jobs Act ~~(" TCJA ")~~, federal net operating losses (" NOL ") incurred in taxable years beginning after 2017 and in future years may be carried forward indefinitely, but the

deductibility of such federal NOLs for taxable years beginning after 2020 is limited. In addition, under Section 382 of the **Internal Revenue** Code **of 1986** , our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we experience an " ownership change. " Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who ~~owns~~ **own** at least 5 % of a corporation' s stock within a specified testing period. Similar rules may apply under state tax laws. We **are conducting a Section 382 study, which is still subject to finalization, but which** may ~~have~~ **show that we** experienced an ownership change **in** ~~as a result of the August 2020 underwritten public offering of our common stock and / or the February~~ 2024 **. If such** ~~private placement of shares of common stock and pre- funded warrants, and may in the future experience~~ ownership ~~changes~~ **change** ~~from future offerings or~~ **has occurred, up to** ~~other~~ **the vast majority** ~~changes in the ownership of our stock. As a result, the amount~~ of the NOLs **, capital losses** and research credit carryforwards presented in our **consolidated** financial statements ~~could~~ **would** be ~~limited~~ **subject to limitations** and **therefore** may expire unutilized. In addition, ~~state~~ **states** ~~suspensions of~~ **may suspend** the ability to use NOLs ~~,~~ and research credits ~~, may~~ **which could further** limit our ability to use our NOLs and research credits to offset state taxable income and taxes **. For example, California has enacted legislation that, with certain exceptions, suspends the ability to use California net operating losses to offset California income and limits the ability to use California business tax credits to offset California taxes, for taxable years beginning on or after January 1, 2024, and before January 1, 2027. Potential natural disasters, some possibly related to the increasing effects of climate change, could damage, destroy or disrupt operations at our office and laboratories, CMO premises, study sites, and / or other third- party vendor sites, which could have a significant negative impact on our operations. We are vulnerable to the increasing impact of climate change and other natural disasters. Volatile changes in weather conditions, including extreme heat or cold, could increase the risk of wildfires, floods, blizzards, hurricanes and other weather- related disasters. Such extreme weather events, or other natural disasters such as earthquakes, can cause power outages and network disruptions that may result in damage, destruction or disruption to operations at our offices, laboratories, CMO premises, or other third- party vendor sites and may impact our ability to continue or complete our clinical studies or to produce, characterize or otherwise develop our product candidate which could negatively impact our operations and delay our plans to commercialize our product candidates. They could also cause significant damage to or destruction of our clinical study sites resulting in temporary or long- term closures of these facilities. Such disasters could also result in loss or damage to our office buildings, laboratories, CMO premises, employee and / or patient homes, employees and / or patients relocating to other parts of the country or being unwilling to travel to the clinical study site locations, and the inability to recruit key employees and / or enroll patients. This could result in adverse impacts to the available workforce and / or patient enrollment in our clinical studies, damage to or destruction of materials and / or data, or the inability to conduct clinical studies and deliver new data** . Risks Related to Our Common Stock The trading price of the shares of our common stock has been and could continue to be highly volatile, and purchasers of our common stock could incur substantial losses. Our stock price has been and is likely to continue to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including those discussed above and others such as: • our ability to enroll and dose subjects in any clinical trials that are on- going, or that we plan to conduct in the future; • our ability to obtain regulatory approvals for our product candidates and delays or failure to obtain such approvals; • our plans to conduct nonclinical studies to determine the best gene therapy candidates to advance in development; • results of any clinical trials of our product candidates and the results of trials of competing product candidates or of other companies in our market sector; • investor perception and analysis of the results of our clinical trials, which may be different than our own; • regulatory developments in the U. S. and foreign countries; • our financial results, variations in our financial results and the adequacy of our cash runway to achieve key milestones, or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems, especially in light of current reforms to the U. S. healthcare system; • announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments; • failure to maintain our existing third- party license and collaboration agreements; • delays in manufacturing adequate supply of our product candidates; • adverse publicity relating to gene therapy and to biotechnology generally, including with respect to other products and potential products in such markets; • market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations; • sales of our stock by insiders and stockholders; • trading volume of our common stock; • general economic, industry and market conditions other events or factors, many of which are beyond our control; • additions or departures of key personnel; and • intellectual property, product liability or other litigation against us. In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies following periods of volatility in the market prices of these companies' stock, and similar litigation has been instituted against us. Such litigation could cause us to incur substantial costs and divert management' s attention and resources, which could have a material adverse effect on our business, financial condition, results of operations and prospects. If we sell shares of our common..... prefer to develop and market ourselves. Anti- takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include: • the authorization of the issuance of " blank check " preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval; • the limitation of the removal of directors by the stockholders; • a staggered board of directors; • the prohibition of stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders; • the elimination of the ability of stockholders to call a special meeting of stockholders; • the ability of our board of directors to accelerate the

vesting of outstanding option grants, restricted stock units or other equity awards upon certain transactions that result in a change of control; and • the establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 % of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. We **have identified a material weakness in our internal control over financial reporting. If we** are ~~obligated~~ **unable** to ~~develop and~~ **remedy the material weakness, or if we fail to** maintain ~~proper and~~ **an effective system of internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in our company and, as a result, the value of our common stock. The Sarbanes- Oxley Act requires, among other things, that we maintain** effective internal control over financial reporting **and disclosure** ~~. In the future, we may not complete our execution of our internal control over financial reporting in a timely manner, or these internal~~ controls ~~may not be determined to be effective, which may result in material misstatements in our consolidated financial statements~~ and **procedures** ~~may adversely affect investor confidence in our company and, as a result, the value of our common stock~~ . We are required, pursuant to Section 404 of the Sarbanes- Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. Complying with Section 404 requires a rigorous compliance program as well as adequate time and resources. We may not be able to complete our internal control evaluation, testing and any required remediation in a timely fashion. **As** ~~Additionally, if we identify one or~~ more **fully described in Part II, Item 9A, in connection with our preparation of the consolidated financial statements for the year ended December 31, 2024 we have identified non- cash errors in the accounting for tenant improvement allowances that resulted in the restatement of our consolidated financial statements as of and for the year ended December 31, 2023, as well as the unaudited condensed consolidated quarterly financial information for the quarterly periods in the years ended December 31, 2023 and 2024. These errors were indicative of a** material ~~weaknesses~~ -- **weakness** in our ~~internal control~~ **controls** over ~~financial reporting~~ **lease accounting as of December 31 , 2024** ~~we will not be able to assert that our internal controls are effective~~ . A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the Company' s annual or interim financial statements will not be prevented or detected on a timely basis. ~~As~~ **We previously identified a material weakness as** of December 31, 2022, **related** ~~we identified a deficiency in the operating effectiveness of controls in our financial statement close process that we considered~~ to ~~be~~ a ~~material weakness. An immaterial~~ non- cash lease accounting error ~~was identified~~ **related to another operating lease** in previously issued financial statements. ~~While the~~ **We have also** identified ~~error was not material, we considered the~~ **other** ~~magnitude of the potential errors that could arise from the operating deficiency as potentially material. This material weakness did not result in the restatement of prior quarterly or annually filed financial statements. During 2023, management conducted a remediation plan to address its material weakness, which included increasing the rigor with which management evaluates the accounting of material non- routine transactions by engaging additional outside financial reporting and technical accounting expertise. As of December 31, 2023, we have remediated the material weakness related to our internal controls~~ -- **control deficiencies** ~~over financial reporting that were determined to be ineffective as of December 31, 2022~~ . **We** ~~Even though we remediated this material weakness as of December 31, 2023, we~~ cannot be certain that ~~other~~ **additional** material weaknesses and control deficiencies will not be discovered in the future. If our efforts **to remediate the material weakness** are not successful **,** ~~or other~~ material weaknesses are identified in the future or we are not able to comply with the requirements of Section 404 in a timely manner, our reported financial results could be materially misstated, and we could be subject to investigations or sanctions by regulatory authorities, which would require additional financial and management resources, and the value of our common stock could decline. To the extent we identify future weaknesses or deficiencies, there could be material misstatements in our consolidated financial statements **,** and we could fail to meet our financial reporting obligations. As a result **of failure to remediate the material weakness or future weaknesses or deficiencies** , our ability to obtain additional financing, or obtain additional financing on favorable terms, could be materially and adversely affected **,** which, in turn, could materially and adversely affect our business, our financial condition and the value of our common stock. If we are **or remain** unable to assert that our internal control over financial reporting is effective in the future, investor confidence in the accuracy and completeness of our financial reports could be further eroded, which would have a material adverse effect on the price of our common stock. Our quarterly operating results may fluctuate significantly. We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, which may include: • variations in the level of expenses related to our clinical trial and development programs; • addition, termination or modification of clinical trials; • any intellectual property infringement lawsuit or other litigation in which we may become involved; • regulatory developments affecting our product candidates; • our execution of any collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements; • the nature and terms of stock- based compensation grants; and • derivative instruments recorded at fair value. If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. Our certificate of incorporation and bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America. will be the exclusive forums for substantially all 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 provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: • any derivative action or proceeding brought on our behalf; • any action asserting a breach of fiduciary duty; • any action asserting a claim against us arising under the Delaware General Corporation Law; and • any action asserting a claim against us that is governed by the internal- affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated bylaws provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our certificate of incorporation and bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. These exclusive forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive- forum provision in our certificate of incorporation or bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business. ~~81~~