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

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Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this annual report and in our other public filings in evaluating our business. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock. Risk Factors Summary Our ability to execute on our business strategy is subject to a number of risks and uncertainties, including those outside of our control, that could cause our actual results to be harmed, including risks regarding the following: • We are early in our development efforts, with a limited operating history, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and future viability. • We have not generated any product revenue to date, have incurred significant net losses since our inception, and expect to continue to incur significant net losses for the foreseeable future. • Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates, if approved. • We require substantial additional capital to finance our operations, which if available, may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and / or eliminate one or more of our research and drug development programs or future commercialization efforts. • Our **loan agreement with Silicon Valley Bank (SVB), a division of First- Citizens Bank & Trust Company (the Loan Agreement), requires us to comply with specified operating covenants and places restrictions on our operating and financial flexibility. • Our** product candidates are in the early stages of development **,** and we have no products approved for commercial sale. If we are unable to successfully develop, receive regulatory approval for, manufacture and commercialize our product candidates, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed. • We intend to identify and develop gene therapy product candidates based on novel technology, and because the regulatory landscape that governs any product candidates we may develop is rigorous, complex, uncertain and subject to change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop. • The mechanisms of action of our product candidates are unproven, and we do not know whether we will be able to develop any drug of commercial value. • Drug development involves a lengthy and expensive process with an uncertain outcome. The preclinical studies, clinical trials and post- marketing studies of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA, **European Medicines Agency (** EMA **)** or other comparable foreign regulatory authorities or otherwise produce positive results and the results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. • Our product candidates may cause serious adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could delay or prevent regulatory approval, or market acceptance, or even if approval is received, require them to be taken off the market, include new safety warnings, contraindications or precautions, or otherwise limit their commercial potential or result in significant negative consequences. • Due to the significant resources required for the development of product candidates, and depending on our ability to access capital, we must prioritize development of certain programs and product candidates. Moreover, we may expend our limited resources on programs or product candidates that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. • Due to our limited manufacturing experience **,** there can be no assurance that we will be able to successfully manufacture product candidates to support our clinical development and commercialization plans. • The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval of our product candidates, we will be unable to generate product revenue and our business will be substantially harmed. • If we are unable to obtain, maintain, protect, defend and enforce patent and other intellectual property coverage for our technology and product candidates, our competitors could develop and commercialize technology and product candidates similar or identical to ours, and our ability to commercialize our technology and product candidates may be adversely affected. • Our commercial success depends significantly on our ability to operate without infringing, misappropriating or otherwise violating the patents and other intellectual property and proprietary rights of third parties. • We rely on third parties to conduct our preclinical studies and our clinical trials, and plan to rely on third parties to conduct such future drug development activities. These third parties may not perform satisfactorily, including failing to meet completion deadlines, or to comply with applicable regulatory requirements, which may harm our business. Risks Related to Our Financial Position, Need for Additional Capital and Limited Operating History We are early in our development efforts, with a limited operating history and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and future viability. We have limited experience conducting clinical trials, have no products approved for commercial sale and have not generated any revenue. We are developing therapies that address the underlying drivers of heart disease, which is an unproven and highly uncertain undertaking and involves a substantial degree of risk. Since our inception, we have devoted substantially all of our focus and financial resources to identifying and

developing product candidates, conducting preclinical studies and clinical trials, developing our internal capabilities, acquiring technology, organizing and recruiting management and technical staff, business planning, establishing our intellectual property portfolio, raising capital, and providing general and administrative support for these operations. We have not yet demonstrated our ability to successfully complete any late- stage clinical trials, obtain marketing approvals, manufacture a late stage clinical- or commercial- scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for investors to accurately predict our likelihood of success and viability than it could be if we had a longer operating history. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early- stage biotechnology companies in rapidly evolving fields. We also may need to transition from a company with a research and development focus to a company capable of supporting commercial activities. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer. We have incurred significant net losses since our inception, have not generated any product revenue to date and have financed our operations principally through issuances of our stock. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~403~~ **514** . ~~3~~ **4** million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs, manufacturing activities and from general and administrative costs associated with our operations. Our product candidates will require substantial additional development time and resources before we will be able to apply for regulatory approvals and, if approved, begin generating revenue from product sales. As a result, we expect that it will be several years, if ever, before we receive approval to commercialize a product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to discover, develop and market additional potential products. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter such that a period- to- period comparison of our results of operations may not be a good indication of our future performance, particularly since we expect our expenses to increase if and when our product candidates progress through late- stage clinical development, where costs may increase significantly. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital, our ability to fund the development of our product candidates and our ability to achieve and maintain profitability and the performance of our stock. Our business depends on the successful research, development, manufacturing, regulatory approval and commercialization of product candidates that we discover. Our ability to generate revenue and achieve profitability depends significantly on our ability, or any future collaborator' s ability, to achieve several objectives, including: • successful and timely completion of preclinical and clinical development of product candidates and programs, including, but not limited to, generating sufficient data to support the initiation or continuation of clinical trials; • submission of INDs or other regulatory applications for our planned clinical trials, obtaining regulatory approval to commence clinical trials of our product candidates, and achieving favorable results from clinical trials; • establishing and maintaining relationships with **contract research organizations (** CROs **)** and clinical sites for the clinical development of our product candidates; • the initiation and successful patient enrollment and completion of clinical trials on a timely basis; • acceptable frequency and severity of adverse events in the clinical trials; • ~~the~~ efficacy and safety profiles that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval; • timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development; • complying with any required post- marketing approval commitments to applicable regulatory authorities; • operating a manufacturing facility and developing an efficient and scalable manufacturing process for our product candidates, and the timely manufacture of sufficient quantities of a product candidate for use in clinical trials and, if approved, commercialization; • establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for our product candidates, if approved; • successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in- house or with one or more collaborators; • successful outputs from our capsid engineering and promotor and ~~regulator~~ **regulatory** elements efforts; • a continued acceptable safety profile following any marketing approval of our product candidates; • ~~the~~ actual market- size, ability to identify patients and the demographics of patients eligible for our product candidates, which may be different than expected; • commercial acceptance of our product candidates by patients, the medical community and third- party payors; • our ability to distribute our products to certain segments of the patient population only accessible through restricted or closed distribution channels; • satisfying any required post- marketing approval commitments to applicable regulatory authorities, and maintaining consistent quality, purity, and potency across clinical supplies and commercial supplies for any approved products; • identifying, assessing and developing new product candidates, and our ability to expand into multiple indications; • obtaining, maintaining, and expanding patent and other intellectual property protection, trade secret protection and regulatory exclusivity, both in the U. S. and internationally; • protecting and enforcing our rights in our intellectual property portfolio; • defending against third- party infringement, misappropriation, or other claims, if any; • entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates and to meet our obligations set forth under such arrangements; • obtaining coverage and adequate reimbursement by third- party payors for our products and patients' willingness to pay in the absence of such coverage and adequate reimbursement; • obtaining additional funding to develop, manufacture and commercialize our product candidates; • addressing any competing therapies and technological and market developments; • managing costs, including any unforeseen costs, that we may incur as a result of nonclinical study or clinical trial delays; and • attracting, hiring and retaining qualified and key personnel including clinical, scientific, management and administrative personnel. We may never be successful in achieving our objectives and, even if we

are, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations. We require substantial additional capital to finance our operations, which, if available, may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and / or eliminate one or more of our research and drug development programs or future commercialization efforts. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time- consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in the near- and long- term in connection with our ongoing activities, particularly as we initiate and conduct clinical trials of, and seek marketing approval for, our product candidates. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA, EMA or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the design and outcome of our planned preclinical studies and clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. We also expect to incur costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations. As of December 31, ~~2023~~ **2024**, we had $ ~~104~~ **61**. ~~6~~ **4** million in cash, cash equivalents and investments in marketable securities. We may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day- to- day activities, which may adversely affect our ability to develop our product candidates. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our preclinical development programs, platforms, manufacturing activities, ongoing or planned clinical trials or future commercialization efforts. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, maintaining certain leverage ratios, making acquisitions, engaging in acquisition, merger or collaboration transactions, selling or licensing our assets, making capital expenditures, redeeming our stock, making certain investments, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions **, including those in our Loan Agreement,** could adversely impact our ability to conduct our operations and execute our business plan. If we raise additional funds through upfront payments or milestone payments pursuant to strategic collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or intellectual property, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings, we may be required to delay, limit, reduce or terminate 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 **. Our Loan Agreement requires us to comply with specified operating covenants and places restrictions on our operating and financial flexibility. As of the filing date of this periodic report, under our Loan Agreement, we have the right to draw down $ 22. 5 million at our discretion, up to an additional $ 2. 5 million, subject to specified conditions, and up to an additional $ 20. 0 million may be made available to us at the lender' s sole discretion. Our ability to draw down an additional tranche commitment of $ 2. 5 million is subject to our achievement, as determined by SVB in its discretion, of a clinical milestone or the receipt of specified proceeds from equity financings and other qualified funding. Our ability to draw down an additional tranche of $ 20. 0 million is subject to agreement on the terms and conditions thereof and SVB' s sole discretion. As security for our obligations under the Loan Agreement, we granted SVB a first priority security interest on substantially all of our assets (other than intellectual property), subject to certain exceptions. We intend to satisfy our future debt service obligations with our existing cash and cash equivalents. However, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our outstanding debt. Funds from external sources may not be available on acceptable terms, if at all. The Loan Agreement contains customary representations and warranties, events of default and affirmative and negative covenants, including covenants that limit or restrict our ability to, among other things, dispose of assets, make changes to our business, merge or consolidate, incur additional indebtedness, incur additional liens, pay dividends or other distributions or repurchase equity, make investments, and enter into certain transactions with affiliates, in each case subject to certain exceptions. These restrictive covenants could limit our flexibility in operating our business and our ability to pursue business opportunities that we or our stockholders may consider beneficial. In addition, a failure to comply with the conditions of our Loan Agreement, including a breach of any covenant, could limit our ability to draw upon available tranches or result in an event of default and an acceleration of any outstanding loans thereunder. In the event of an acceleration of amounts due under our Loan Agreement as a result of an event of default, including upon the occurrence of an event or circumstance that could be expected to have a material adverse effect on our business, operations, properties, assets or financial condition or a failure to pay any principal or interest due, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and SVB could seek to enforce security interests in the collateral**

securing such indebtedness. Even if we are able to repay such accelerated debt amount under the Loan Agreement, the repayment of these sums may significantly reduce our working capital and impair our ability to operate as planned. As such, any declaration by SVB of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. Further, if we are liquidated, SVB' s rights to repayment under the Loan Agreement would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation . Our ability to utilize our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be limited. Our net operating loss (NOL) carryforwards may be unavailable to offset future taxable income because of restrictions on their use under U. S. tax law. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended ~~(Code)~~ , if a corporation undergoes an " ownership change " (generally defined as a cumulative change in the corporation' s ownership by " 5- percent shareholders " that exceeds 50 percentage points over a rolling three- year period), the corporation' s ability to use its pre- change NOLs and certain other pre- change tax attributes to offset its post- change taxable income may be limited. Similar rules may apply under state tax laws. We have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. **In addition, the use of our NOLs and other tax attributes may be subject to other limitations under applicable law. For example, California has recently enacted a temporary suspension on the use of state NOLs in taxable years beginning in 2024, 2025 and 2026, which would adversely affect our company if we earn taxable income in the impacted tax years.** Consequently, our ability to use our NOLs and certain other tax attributes may be limited. Risks Related to the Discovery, Development, Manufacturing and Commercialization of Our Product Candidates Before we are able to generate any revenue from product sales, each of our programs and product candidates will require additional preclinical and / or clinical development, expansion of manufacturing capabilities and expertise, regulatory approval, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts. Consequently, because of the substantial operational and financial investment required to further develop and commercialize our product candidates, there is a high risk of failure and we may never succeed in developing marketable products. If we are unable to optimize our manufacturing processes to produce product candidates that meet applicable regulatory standards, do not successfully initiate and complete our clinical trials in a timely manner or fail to achieve favorable results from our trials, we may experience significant delays or be unable to advance our programs. We cannot be certain that our clinical trials will be initiated and completed on time, if at all, or whether our planned clinical strategy will be acceptable to the FDA or comparable foreign regulatory authorities. Furthermore, any changes to our development programs may cause our product candidates to perform differently and affect the results of planned clinical trials, which 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. There is a high failure rate for biopharmaceutical products proceeding through clinical trials. It is not uncommon for product candidates to exhibit unforeseen safety issues or inadequate efficacy when tested in humans despite promising results in preclinical animal models or earlier clinical studies. In addition, a number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials and we may experience the same. We may also encounter regulatory delays or rejections as a result of many factors, including varying interpretations of data or changes in regulatory policy during the period of product development. Because of the early stage of development of our programs, our ability to eventually generate significant revenues from our product candidates, which we do not expect will occur for several years, if ever, will depend on a number of factors, including those described in the Risk Factor entitled " Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates, if approved. " We do not have control over many of these factors, including certain aspects of the manufacturing process, preclinical and clinical development, the regulatory review process and potential threats to our intellectual property rights. If we are not successful with respect to one or more of these factors, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. To become and remain profitable, we must develop, obtain approval for and eventually commercialize product candidates that generate significant revenue. We do not expect to receive approval of any product candidates for many years and may never succeed in these activities. Even if we obtain approval and begin commercializing one or more of our product candidates, we may never generate revenue that is significant enough to achieve profitability, as we will continue to incur substantial research and development, manufacturing and other expenditures to develop and market additional product candidates. Even if we successfully discover and advance product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this " Risk Factors " section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, manufacture, commercialize or generate significant revenue from any product candidates. We intend to discover, develop, manufacture, and commercialize gene therapy product candidates for the heart. Our product candidates may use both known capsids, such as AAV9, as well as proprietary capsids developed in- house through our own capsid engineering efforts or licensed from third parties. Furthermore, our product candidates may also use novel heart- specific promoters and we may explore different routes- of- administration involving infusion- or injection- based catheters to support targeted delivery and efficient uptake of gene therapies for the heart. We are also establishing proprietary manufacturing processes for our product candidates. Our future success depends on the successful development of these novel therapeutic approaches. Within the broader genetic medicine field, very few therapeutic products, including those that utilize AAV- mediated gene transfer, have received marketing authorization from the FDA, EMA or comparable foreign regulatory authorities. No AAV- based gene therapies have yet been approved for the heart, much less therapies for the heart using novel capsids or promoters or delivery methods. It is therefore difficult to determine how long it will take, how much it will cost, or how likely it will be to obtain

regulatory approvals for our product candidates in the U. S., EU or other jurisdictions. The regulatory requirements that will govern any novel gene therapy product candidate we develop are not entirely clear, have changed over time and are subject to further change. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Changes in the regulatory authorities' data requirements and risk mitigation methods, including requirements resulting from safety concerns raised by regulatory authorities in clinical programs of unrelated companies in the gene therapy and cardiovascular fields in general, could have a material impact on our clinical development, increase our costs, and delay or preclude regulatory approval of our product candidates. Moreover, there is substantial overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the U. S., the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research (CBER) to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Our product candidates will need to meet safety and efficacy standards applicable to any new biologic under the regulatory framework administered by the FDA. In addition to FDA oversight and oversight by IRBs, under guidelines promulgated by the National Institutes of Health (NIH), gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee (IBC), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many clinical study sites receive NIH funding and many companies and other institutions not otherwise subject to the NIH guidelines voluntarily follow them. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the EU. The EMA' s Committee for Advanced Therapies (CAT) is responsible for assessing the quality, safety, and efficacy of advanced- therapy medicinal products. Advanced- therapy medicinal products include gene therapy medicines, somatic- cell therapy medicines and tissue- engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the EU, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products in the EU may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point. Furthermore, approvals by the EMA may not be indicative of what the FDA may require for approval. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approvals necessary to bring a potential gene therapy product to market could decrease our ability to generate sufficient product revenue and our business, financial condition, results of operations and prospects could be materially harmed. Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy and gene regulation products may cause the FDA, EMA, and other regulatory bodies to revise the requirements for the conduct of the clinical trials and approval of our product candidates or limit the use of products utilizing gene regulation technologies, either of which could harm our business. For example, the FDA has imposed clinical holds on various clinical trials of gene therapy product candidates being developed by other companies. In addition, the clinical trial requirements of the FDA, EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel potential treatments for diseases in which, in some cases, there is little clinical experience with potential new endpoints and methodologies, there is heightened risk that the FDA, EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. In addition, we may not be able to identify or develop appropriate animal disease models to enable or support planned clinical development. Any natural history studies that we may conduct or rely upon in our clinical development may not be accepted by the FDA, EMA or other regulatory authorities. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene regulation technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval. The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates, or lead to significant post- approval limitations or restrictions. As we advance our research programs and develop our product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our product candidates in a timely manner, if at all. We have discovered and are developing product candidates that have what we believe are novel mechanisms of action. Because no currently-approved drugs appear to operate via the same biochemical mechanisms as our compounds, we cannot be certain that our product candidates will result in commercially viable drugs that safely and effectively treat the indications for which we intend

to develop them. The results we see for our compounds in preclinical models may not be replicated in subsequent preclinical studies or translate into similar results in humans in clinical trials, and results of early clinical trials in humans may not be predictive of the results of larger clinical trials or post- marketing studies that may later be conducted with our product candidates. As an example, patients may develop antibodies against the product candidates, or the product candidates may otherwise have a more limited duration of therapeutic effect than anticipated, resulting in decreased efficacy over time, which could delay approval and, if approved, limit the ultimate commercial value. Even if we are successful in developing and receiving regulatory approval for a product candidate for the treatment of a particular disease, we cannot be certain that it will be accepted by prescribers or be reimbursed by insurers or that we will also be able to develop and receive regulatory approval for that or other product candidates for the treatment of other diseases. If we are unable to successfully develop and commercialize our product candidates, our business will be materially harmed. Moreover, in the event any of our competitors were to develop their own product candidates that have a similar mechanism of action to any of our product candidates, any efficacy or safety concerns identified during the development of such similar product candidates may have an adverse impact on the development of our product candidates. For example, if our competitors' product candidate having a similar mechanism of action as any of our product candidates is shown in clinical trials to give rise to serious safety concerns or have poor efficacy when administered to the target patient population, the FDA or other regulatory bodies may subject our product candidates to increased scrutiny, leading to additional delays in development and potentially decreasing the chance of ultimate approval of our product candidates. **Drug development involves a lengthy and expensive process with an uncertain outcome. The preclinical studies, clinical trials and post- marketing studies of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results and the results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.** Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is uncertain. We cannot guarantee that any of our preclinical studies or clinical trials will be initiated, conducted or completed on schedule or as planned, or at all. Failure can occur at any stage of testing. Such failure may result from a multitude of factors, including, among other things, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria, novel assay design and failure to demonstrate favorable safety or efficacy traits, which could delay or prevent the submission of an IND or CTA, initiation of a clinical trial, receipt of marketing approval or our ability to commercialize our product candidates, or require us to suspended or terminate further development of our product candidates. Moreover, the outcome of preclinical studies and early- stage clinical trials may not be predictive of the success of later clinical trials. For example, our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. As a result, we cannot assure you that any preclinical studies, clinical trials or post- marketing studies that we conduct will demonstrate consistent or adequate efficacy and safety to support marketing approval. Further, FDA and other regulatory authorities may implement new policies and regulations on clinical trials. For example, the EU Clinical Trials Regulation (CTR), which repealed the EU Clinical Trials Directive, became applicable on January 31, 2022, and provided a three- year transition period. The CTR streamlined the processes for applying for authorization and supervision of clinical trials in the EU. ~~Any clinical~~ **From January 31, 2025, any** ~~trial~~ **trials approved under the Clinical Trials Directive that continue running will need to comply with the CTR, and their sponsors must enter information on the trials in the Clinical Trials Information System. Trials** we initiate in the **United Kingdom are also** ~~EU in the future will become~~ subject to ~~the provisions~~ **regulatory requirements and policies** of the ~~CTR~~ **MHRA** . Compliance with the CTR **and / or MHRA** requirements by us, our collaborators and third- party service providers, such as contract research organizations, may increase our clinical trial costs and impact the timeline of our development plans. If we are slow or unable to adapt to changes in clinical trial requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be negatively impacted. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials even after achieving promising results in preclinical testing and earlier- stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs. This is particularly true for clinical trials in very rare diseases, such as with certain indications we are pursuing, where the very small patient population makes it difficult or impossible to conduct two traditional, adequate and well- controlled studies, and therefore the FDA or comparable foreign regulatory authorities are often permitted to exercise flexibility in approving therapies for such diseases. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or comparable foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates and / or cause the FDA or comparable regulatory authorities to require additional testing before approving any of our product candidates. We may experience numerous unforeseen events during, or as a result of, preclinical studies, clinical trials or post- marketing studies that could delay or prevent receipt of marketing approval or our ability to commercialize our product candidates, including: • inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of clinical trials; • delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials; • receipt of feedback from regulatory authorities that requires us to modify the design of our preclinical or clinical trials; • preclinical study or clinical trial

observations or results that require us to modify the design of our clinical trials; • negative or inconclusive preclinical study or clinical trial results that may require us to conduct additional preclinical studies or clinical trials or abandon certain research and / or drug development programs; • extended IRB, IBC and / or EC review process, or inability to obtain approval from one or more of these committees; • the number of patients required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated, participants dropping out of these clinical trials at a higher rate than anticipated, or more patients failing to meet eligibility criteria than anticipated; • any failure or delay in reaching an agreement with CROs and clinical trial sites; • the suspension or termination of our clinical trials, as a result of a clinical hold by regulatory authorities or a voluntary pause, for various reasons, including a finding that our product candidates have undesirable side effects or other unfavorable or unexpected characteristics or risks or non- compliance with regulatory requirements; • changes to clinical trial protocol; • clinical sites deviating from trial protocol or dropping out of a trial; • the costs **and / or duration** of preclinical studies or clinical trials being greater than anticipated; • the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates being insufficient or inadequate or slower than anticipated; • subjects experiencing serious, severe, unexpected or otherwise important drug- related or study- related adverse effects; • selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data; • inaccurate clinical data entry or reporting by clinical sites; • variability of efficacy assessments; • a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMPs, regulations or other applicable requirements, or infections or cross- contaminations of product candidates in the manufacturing process; • any changes to our manufacturing process that may be necessary or desired; • third- party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP or other regulatory requirements; • **CROs and other** third- party contractors not performing data collection or analysis in a timely or accurate manner; • third- party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities 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; • regulators revising the requirements for approving our product candidates; • an unsuccessful post- marketing study or failure to complete such a study; • absence in some countries of established groups with sufficient regulatory expertise for review of AAV gene therapy protocols; and • the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment. To the extent we pursue any pediatric indications or expand any approved drug product labeling to include pediatric populations, we may face additional challenges associated with clinical testing in pediatric populations, which can increase our operational costs, delay regulatory approval and commercialization, or expose us to additional liability. For example, finding qualified clinical sites that have access to sufficient pediatric populations and that are interested in participating in our clinical trials may take more time than adult indications. There may be fewer eligible patients with the target genetic disorder or heart disease or condition applicable to our product candidate for our planned clinical trials. This may increase the time needed to enroll patients for our planned pediatric clinical trials, increase our clinical development timelines, delay approval for such pediatric indications, and increase our operational costs. We may also be required to modify the formulation or other aspects of the product candidate, as compared to the comparable product candidate intended for adult patient populations, make manufacturing changes, modify route of administration, and conduct additional clinical trials, such as bridging studies and additional safety studies before we can commence our clinical trials in pediatric populations. The FDA or other health authorities may require us to complete studies in adults prior to initiating testing in children. Any delays in our planned clinical development activities for pediatric patients could have an adverse effect on our business operations. If we are required to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete preclinical studies or clinical trials of our product candidates or other testing in a timely manner and if the results of these studies, trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs and be delayed in submitting an IND, initiating clinical trials or seeking and obtaining marketing approval. We may also decide to change the design or protocol of one or more of our planned clinical trials, which could result in increased costs and expenses and / or delays. Any delays in initiating or completing our preclinical studies or clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues, including by shortening any period during which we may have the exclusive right to commercialize our product candidates and permitting our competitors to bring products to market before we do. If we receive approval, it is possible that we may receive limited or restrictive marketing approval, be subject to additional post- marketing testing requirements or have the drug removed from the market after obtaining marketing approval. Moreover, in the future, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates, which may harm our business, financial condition and prospects significantly. Our product candidates may cause serious adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could delay or prevent regulatory approval or market

acceptance, or even if approval is received, require them to be taken off the market, include new safety warnings, contraindications or precautions, or otherwise limit their commercial potential or result in significant negative consequences. We are developing novel therapies for the treatment of heart disease. As a result, there is uncertainty as to the safety profile of product candidates we may develop. Patients in our clinical trials have suffered and may continue to suffer adverse events, including serious adverse events or other side effects, including those not observed in our preclinical studies or previous clinical trials. Patients treated with our product candidates may also be undergoing other therapies or procedures which can cause side effects or adverse events that are unrelated to our product candidates but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events, either during the course of or after participating in such trials. These events may be due to one or more factors, including, without limitation, **the underlying heart disease,** other therapies or medications that such patients may be using, the drug product formulation of our product candidates, complications arising from protocol regimens, the method of delivery of our product candidates or ~~simply due to the~~ **other diseases the** ~~gravity of such~~ patients **have** ~~' illnesses~~ . In some cases, it may not be clear if an adverse event is due to the product candidate, another therapy, the underlying disease, or another cause, and causality may be incorrectly attributed to the product candidate. Serious adverse events or other side effects observed in any of our clinical trials, or similar trials by other sponsors, may result in difficulty recruiting patients to the clinical trials, cause patients to drop out of our trials, or require that we abandon the trials or our development efforts of that product candidate altogether. We, the FDA, EMA, other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects or that the expected benefit does not justify the risk. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early- stage trials have later been found to cause side effects that prevented their further development. There is no guarantee that our product candidates will not have side effects similar to those seen in other gene therapies or that we will be able to prevent such side effects from escalating to an unsafe level for our patients. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies, result in marketing approval with restrictive label warnings or for limited patient populations, or result in potential product liability claims. Any of these developments could materially harm our business, financial condition and prospects. Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. No regulatory agency has made any determination that any of our product candidates or discovery programs is safe or effective for use by the general public for any indication. We cannot predict whether our product candidates will cause toxicities in humans that would preclude regulatory approval, ~~of~~ **or** if approved, lead to the revocation of regulatory approval based on preclinical studies or early- stage clinical trials. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities. We will be required to demonstrate with substantial evidence through well- controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early- stage clinical trials does not mean that future clinical trials will be successful. For instance, we do not know whether any of our product candidates will perform in our current or future preclinical studies or future clinical trials as it has in prior preclinical studies or earlier clinical trials. Product candidates in clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, EMA and other comparable foreign regulatory authorities despite having progressed through preclinical studies. Regulatory authorities may also limit the scope of later- stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates, or prevent regulatory approval. In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product candidates may also be undergoing other therapies and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes and success in one trial does not ensure success in the next. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain approval to market any of our product candidates. If we experience delays or difficulties in the enrollment and / or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to such trial' s conclusion. Patient enrollment and retention are significant factors in the timing of clinical trials and our ability to enroll eligible patients may be limited or slower than we anticipate. We are developing product candidates for the treatment of heart disease, including for certain indications, such as rare genetic diseases, that have limited patient pools from which to draw for clinical trials. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for our planned clinical trials and monitoring such subjects adequately during and after treatment. The process of finding and diagnosing patients may prove costly. Further, the treating physicians in our clinical trials may also use their medical discretion in advising patients enrolled in our clinical trials to withdraw from our studies to try alternative therapies. Patients also have the right to withdraw from our clinical trials for any reason. Additionally, the FDA,

EMA or other comparable foreign regulatory authorities may require long- term follow- up assessments for a certain number of patients, which could delay marketing approval. We **also** expect patient enrollment to be affected because our competitors have ongoing clinical trials for programs that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials could instead enroll in clinical trials of our competitors' programs. Patient enrollment for our clinical trials **has been and** may **continue to** be affected by other factors, including: • size and nature of the patient population; • the perceived risks and benefits of novel, unproven approaches; • severity of the disease under investigation; • availability and efficacy of approved drugs for the disease under investigation; • ongoing clinical trials evaluating other product candidates in the same disease under investigation; • patient eligibility criteria for the trial in question as defined in the protocol; • perceived risks and benefits of the product candidate under study; • clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or other product candidates being investigated for the indications we are investigating **; • public perception about the use of genetic medicines in human therapeutics or precision medicine** ; • patient referral practices of physicians; • challenges associated with recruiting eligible patients; • the ability to monitor patients adequately during and after treatment; • **limited resources at clinical trial sites, including support for clinical trial enrollment and the availability of hospital beds; •** the activities of key opinion leaders (KOLs) and patient advocacy groups; • proximity and availability of clinical trial sites for prospective patients and the ability of patients to travel to these sites; • the burden of the study protocol on patients, including conflicts with their work, family and personal activities; ~~and~~ • the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may have an advanced disease, will not survive the full terms of the clinical trials **; and • limitations on the rate of patient enrollment required by the clinical trial protocol, including those that may be requested by health authorities** . Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow- up periods. Due to the significant resources required for the development of product candidates, in particular our product candidates in clinical trials, we must decide which programs, product candidates and indications to pursue and advance the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular programs, product candidates or therapeutic areas may not lead to the development of any viable commercial product and may result in the diversion of resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain platforms, programs or product candidates may subsequently also prove to be less than optimal and could cause us to miss valuable opportunities. If we make incorrect **assumptions and / or** determinations regarding **data emerging from our clinical trials,** the viability or market potential of any of our programs or product candidates or misread trends in the biotechnology industry, in particular in the field of cardiology, our business could be seriously harmed. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other programs, product candidates or other diseases that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to our platforms or product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights. We face significant competition and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted. The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. We have competitors both in the U. S. and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start- up companies, universities and other research institutions. We face competition in recruiting personnel, establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in- licensing new product candidates. We expect to face competition from existing products and products in development for each of our programs and anticipate substantial direct competition from a variety of competitors. Many of these current and potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources and commercial expertise than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in- license novel compounds that could make the product candidates that we develop obsolete. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result of all of these factors, our competitors may succeed in obtaining approval from the FDA, EMA or other comparable foreign regulatory authorities or in discovering, developing and commercializing products in our field before we do.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient, have a broader label, are marketed more effectively, are more widely reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain marketing approval from the FDA, EMA or other comparable foreign regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Due to the nature of gene therapy products, use of a competitor gene therapy product by a prospective patient may preclude use of our gene therapy product candidate at a later point in time. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected. **Initial,** ~~Interim~~ **interim** **, and** topline ~~and preliminary~~ data from our clinical trials that we announce or publish may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose ~~preliminary~~ **initial**, interim or topline data from our clinical trials. These ~~interim~~ updates are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following availability of additional data and a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the **initial, interim and / or** topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. **Initial, interim and / or** ~~Topline~~ **topline** data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, **initial, interim and** topline data should be viewed with caution until the final data is available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. **Initial and** ~~Interim~~ **interim** data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between **initial and / or** interim data and final data could significantly harm our business and prospects. Further, additional disclosure of **initial and / or** interim data by us or by our competitors in the future could result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses, may do their own analyses, or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the ~~preliminary~~ **initial, interim** or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects. Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in development or commercialization of our product candidates, limit the supply of our products, if approved, or otherwise seriously harm our business. Our gene therapy product candidates require processing steps that are more complex than those required for most chemical and protein pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we need to employ multiple steps to control our manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, including during the manufacture of drug substance, drug product filling, labeling, packaging, storage and shipping and quality control and testing, could result in product defects, lot failures, product recalls, product liability claims or insufficient inventory. Additionally, we may encounter problems achieving adequate quantities and quality of clinical- grade materials that meet FDA, or other comparable applicable foreign regulatory authorities' standards or specifications with consistent and acceptable production yields and costs. Furthermore, should any of our manufacturing agreements with third parties be terminated for any reason, there are a limited number of manufacturers who would be suitable replacements, and it would take a significant amount of time to transition the manufacturing to a replacement. If we or our third- party manufacturers or suppliers are unable to produce sufficient quantities for preclinical studies or clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects. ~~Due to our limited manufacturing experience, there can be no assurance that we will be able to successfully manufacture product candidates to support our clinical development and commercialization plans.~~ We have fully integrated and internalized AAV manufacturing capabilities to support our gene therapy product candidates. However, to optimize our resources and to utilize extensive third- party experience in small molecule manufacturing, we intend to work with CDMOs for our small molecule programs. Although some of our employees have experience in the manufacturing of biopharmaceutical products from prior employment at other companies, we as a company have limited experience in manufacturing. Furthermore, maintaining manufacturing operations requires significant resources, management time and capital expenditures, particularly in areas relating to operations, quality, regulatory, facilities and information technology. We cannot guarantee that our facility will be able to produce sufficient quantities of product candidates needed to support our preclinical studies and ongoing and planned clinical trials. We may face delays or increased costs in the

production of clinical supply at our manufacturing facility. We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing facility and processes. If we experience unanticipated employee shortage or turnover in any of these areas, we may not be able to effectively manage our ongoing manufacturing operations and we may not achieve the operating efficiencies that we anticipate from developing these capabilities, which may negatively affect our product development timelines or result in difficulties in maintaining compliance with applicable regulatory requirements. Any delays in the ongoing development of our internal manufacturing capabilities may disrupt or delay the supply of our product candidates if we have not maintained a sufficient back- up supply of such product candidates. It may also hamper our ability to further process improvement, maintain quality control, limit our reliance on contract manufacturers and protect our trade secrets and other intellectual property, and could adversely impact the development or commercialization of our product candidates. Moreover, if we were required to change manufacturing facilities during the clinical development process, we may also be required to conduct additional studies, make notifications to regulatory authorities, make additional filings to regulatory authorities, and obtain regulatory authority approval for the new facilities, which approval may be delayed or never received. Our manufacturing facilities will be subject to significant government regulations and approvals, which are often costly and could result in adverse consequences to our business if we fail to comply with the regulations or maintain the approvals. We will need to comply with the FDA' s and applicable foreign regulatory authorities' cGMP requirements for the production of product candidates for clinical trials and, if approved, commercial supply. We will be subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. These requirements include the qualification and validation of our manufacturing equipment and processes. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture of our product candidates as a result of a failure of our facilities or the facilities or operations of our third- party suppliers to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our product candidates, including leading to significant delays in the availability of our product candidates 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 non- compliance 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 or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our product candidates and / or may be subject to product recalls, seizures, injunctions, or criminal prosecution. **Furthermore, regulatory requirements for the manufacturing of genetic medicines may change over time. Our failure to comply with such changes could have a material impact on the manufacturing costs for our product candidates, delay our planned preclinical and clinical trial timelines and / or preclude regulatory approval of our product candidates.** We may not be able to successfully manufacture our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing resulting approved products, if any. To date, our product candidates have been manufactured in quantities adequate for preclinical studies and our Phase 1 clinical trials for our lead product candidates. In order to conduct **later- stage** clinical trials for a product candidate and for commercialization of the resulting product if that product candidate is approved for sale, we will need to manufacture product candidates in larger quantities. We may not be able to successfully repeat or increase the manufacturing capacity for any of our product candidates in a timely or cost- effective manner or at all. Significant changes or scale- up of manufacturing may require additional validation studies, which are costly and which regulatory authorities must review and approve. In addition, quality issues may arise during those changes or scale- up activities. **As** ~~In addition, as~~ product candidates progress through preclinical studies and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize 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 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. **While the manufacturing process alone is complex, quality issues may also arise during drug product filling, labeling, packaging, storage, shipping and ongoing quality control and testing activities.** If we are unable to successfully manufacture any of our product candidates in sufficient quality and quantity, the development of that product candidate and regulatory approval or commercial launch for any resulting products may be delayed or there may be a shortage in supply, which could significantly harm our business. Our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success. Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, third- party payors and others in the medical community. If we are unable to demonstrate sufficient safety or efficacy to permit a broader use of our product candidates, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including: • the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments; • perceived safety and efficacy profile and ease of use for pediatric patient population if approved for a pediatric indication; • the timing of market introduction of the product candidate as well as competitive products; • the clinical indications for which a product candidate is approved; • restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a risk evaluation and mitigation strategy, if any, which may not be required of alternative treatments and competitor products; • physicians, hospitals, treatment centers and patients

considering our product candidates as a safe, pure and effective treatment; • the perceived prevalence and severity of any side effects for our product candidates compared to the prevalence and severity of any side effects for conventional products and other gene therapies; • the potential and perceived advantages of our product candidates over alternative treatments; • the cost of treatment in relation to alternative treatments; • relative convenience and ease of administration; • the willingness of the target patient population or their caregivers to try new therapies and of physicians to prescribe these therapies; • the size of the relevant pediatric patient population if approved for a pediatric indication, including challenges associated with diagnosing or identifying pediatric populations with the applicable target disease or condition; • the availability of coverage and adequate reimbursement by third- party payors, including government authorities; • patients' willingness to pay for these therapies in the absence of such coverage and adequate reimbursement; • the effectiveness of sales and marketing efforts; • support from KOLs and patient advocacy groups **; • negative public perception about the use of genetic medicines, whether related to our technology or our competitor' s technology** ; • unfavorable publicity relating to our product candidates; • the approval of other new therapies for the same indications; and • the acceptance and use of genetic testing required to diagnose the disease and identify patients who qualify for treatment with our product candidates. If any of our product candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted ~~. Adverse public perception or regulatory scrutiny of gene therapy technology or precision medicine for the treatment of heart diseases may negatively impact the developmental progress or commercial success of product candidates that we develop. Gene therapy and precision medicine remain novel technologies. The commercial success of our products, if successfully developed and approved, may be adversely affected by claims that gene therapy or precision medicine is unsafe, ineffective, unethical or immoral. This may lead to unfavorable public perception and the inability of any of our product candidates to gain the acceptance of the public or the medical community. Unfavorable public perceptions may also adversely impact our ability to enroll clinical trials for our product candidates. Moreover, success in commercializing any product candidates that receive regulatory approval will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of such product candidates in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. Publicity of any adverse events in, or unfavorable results of, preclinical studies or clinical trials for our product candidates, or with respect to the studies or trials of our competitors or of academic researchers utilizing similar technologies, even if not ultimately attributable to our technology or product candidates, could negatively influence public opinion. Negative public perception about the use of AAV technology in human therapeutics or precision medicine, whether related to our technology or our competitor' s technology, could result in increased governmental regulation, delays in the development and commercialization of product candidates or decreased demand for the resulting products, any of which may seriously harm our business. It could also negatively impact our ability to raise capital or enter into strategic agreements for the development of our product candidates~~ . The limited number of patients who have the diseases for which our product candidates are being developed may make it more difficult for us to enroll or complete clinical trials or may result in findings in our clinical trials that do not reach levels of statistical significance sufficient for marketing approval. Even if such product candidates achieve marketing approval, because such target patient populations are small and the addressable patient population may be even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth. Some of the indications for which we plan to evaluate our product candidates in clinical trials are rare genetic diseases. Accordingly, there are limited patient pools from which to draw for clinical trials. In addition to the rarity of these diseases, the eligibility criteria of our planned clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their disease is either severe enough or not too advanced to include them in a trial. Moreover, the effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. We may not be able to initiate or continue clinical trials on a timely basis or at all for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Similarly, because some of the conditions we intend to treat are rare in nature, we plan to design and conduct clinical trials utilizing a small number of patients in order to evaluate the safety and therapeutic activity of our product candidates. Conducting trials in smaller subject populations increases the risk that any safety or efficacy issues observed in only a few patients could prevent such trials from reaching statistical significance or otherwise meeting their specified endpoints, which could require us to conduct additional clinical trials, or delay or prevent our product candidates from receiving regulatory approval, which would seriously harm our business. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. Any product candidates we develop may become subject to unfavorable third- party coverage and reimbursement practices, as well as pricing regulations. The availability and extent of coverage and adequate reimbursement by third- party payors including government health administration authorities, private health coverage insurers, managed care organizations and other third- party payors is essential for most patients to be able to afford expensive treatments. The indications we are initially pursuing for our gene therapy product candidates have small patient populations. For product candidates that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such product candidates must be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the U. S. and internationally, on the extent to which the costs of

such product candidates will be covered and reimbursed by third- party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval. There is significant uncertainty related to third- party payor coverage and reimbursement of newly approved products. In the U. S., for example, principal decisions about reimbursement for new products are typically made by the **Centers for Medicare & Medicaid Services (** CMS **)** , an agency within the U. S. Department of Health and Human Services. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third- party payors often follow CMS' s decisions regarding coverage and reimbursement to a substantial degree. However, one third- party payor' s determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate or at the same level of reimbursement. As a result, the coverage determination process is often time-consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third- party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third- party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA- approved drugs for a particular indication. We may need to conduct expensive pharmaco- economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Outside the U. S., the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the EU, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the U. S. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the U. S., the reimbursement for our products may be reduced compared with the U. S. and may be insufficient to generate commercially reasonable revenue and profits. If we are unable to establish or sustain coverage and adequate reimbursement for any product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third- party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage, such inability could have an adverse effect on our business and financial condition. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products. Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. We have limited product liability insurance. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. As clinical trial and product liability insurance becomes increasingly expensive, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition. Also, our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. We may be sued if any of our product candidates **or any medications, procedures or activities associated with our clinical trial protocols** cause or are perceived to cause injury **, or if** ~~or~~ **our product candidates** are found to be otherwise unsuitable during clinical testing, manufacturing, marketing, or sale post- approval. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the **protocol or** product, negligence, strict liability, or a breach of warranties. Claims could also be asserted under state consumer protection laws. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • delays in the development of our product candidates; • FDA, EMA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs; • decreased or interrupted demand for our products; • injury to our reputation; • withdrawal of clinical trial participants and inability to continue clinical trials; • 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 **; • inability to raise capital or enter into strategic agreements for the development of our product candidates** ; • exhaustion of any available insurance and our capital resources; and • the inability to commercialize any products. Risks Related to Regulatory Approval and Other Legal Compliance Matters Our product candidates are and will continue to be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing, distribution and orphan exclusivity of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the U. S. and in many foreign jurisdictions before a new drug can be approved for marketing. Obtaining approval by the FDA, EMA and other comparable foreign regulatory authorities is costly, unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved and the availability of alternative therapies. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. We cannot provide assurance that any of the product candidates we develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them. Applications for our product candidates could be delayed or fail to receive regulatory approval for many reasons, including the following: • the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials; • the FDA, EMA or other comparable foreign regulatory authorities may refuse to accept an application or decide not to accept data from our clinical trials conducted in locations outside of their jurisdiction; • the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use; • the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval; • the FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • the FDA, EMA or other comparable foreign regulatory authorities may require that we conduct additional preclinical studies or clinical trials; • we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that our product candidate' s risk- benefit ratio for its proposed indication is acceptable; • the FDA, EMA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; • the FDA, EMA or other comparable foreign regulatory authorities may fail to approve companion diagnostic tests required for commercialization of our product candidates; and • the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from any particular product candidates we are developing and for which we are seeking approval. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. **If** ~~Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if~~ the FDA or EMA grants marketing approval of a product candidate, **other** comparable regulatory authorities in foreign jurisdictions must ~~also~~ **still** approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. **A** ~~However, a~~ failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the U. S., including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U. S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be harmed. Even if our product candidates receive regulatory approval, such approval may be for a narrower indication than we seek, and our product candidates will be subject to significant post- marketing regulatory requirements and oversight. Even if we eventually complete clinical testing and receive approval for our product candidates, the FDA, EMA and other comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the product' s commercial potential. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the approved uses or indications for which we may market, promote and advertise the drug or the labeling or other restrictions. The regulatory authorities may require precautions or contra- indications with respect to conditions of use or they may grant approval subject to the performance of costly post- marketing clinical trials. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy ~~(REMS)~~ plan as part of approving an NDA **or BLA** , or after

approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. These requirements or restrictions might include 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. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially harm our business, financial condition, results of operations and prospects, and may significantly limit the size of the market for the drug and affect reimbursement by third- party payors. In addition, if the FDA or foreign regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as on- going compliance with cGMP and GCP for any clinical trials that we conduct post- approval. Manufacturers of drug products and their facilities are also subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA, EMA and other comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including: • delays in or the rejection of product approvals; • restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials; • restrictions on the products, manufacturers or manufacturing process; • warning or untitled letters; • civil and criminal penalties; • injunctions; • suspension or withdrawal of regulatory approvals; • product seizures, detentions or import bans; • voluntary or mandatory product recalls and publicity requirements; • total or partial suspension of production; and • imposition of restrictions on operations, including costly new manufacturing requirements. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates, if approved, and generate revenue. Furthermore, non- compliance by us or any future collaborator with regulatory requirements, including safety monitoring and with requirements related to the development of products for the pediatric population can also result in significant financial penalties. **To the extent we** ~~We may not be able to~~ obtain orphan drug **and other** ~~designation~~ **designations from the FDA** ~~or~~ **for** ~~obtain or~~ **our** ~~maintain~~ **product candidates, we may not realize the full benefits of such designations. Further,** orphan drug ~~exclusivity for our product candidates and, even if we do, that~~ exclusivity may not prevent the FDA, EMA or other comparable foreign regulatory authorities, from approving competing products. Regulatory authorities in some jurisdictions, including the U. S. and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals annually in the U. S., or a patient population greater than 200, 000 in the U. S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U. S. Similarly, in the EU, the EC, upon the recommendation of the EMA' s Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life- threatening or chronically debilitating conditions affecting not more than five in 10, 000 persons in Europe and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life- threatening, seriously debilitating or serious and chronic condition. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and without incentives, it is unlikely that sales of the drug in Europe would be sufficient to justify the necessary investment in developing the drug ~~. However, there can be no assurances that we will be able to obtain orphan designations for our product candidates~~ . In the U. S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user- fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the U. S. provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. In view of the court decision in the Catalyst Pharms., Inc. v. Becerra, 14 F. 4th 1299 (11th Cir. 2021) case, in a January 2023 notice, the FDA clarified that while the agency complies with the court' s order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the scope of the orphan- drug exclusivity is limited to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity. The applicable exclusivity period **for an orphan drug** is ten years in ~~Europe~~ **the EU** . The ~~European~~ **EU orphan** exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. **Under the Rare Pediatric Disease Priority Review Voucher program, a sponsor who receives an approval for a drug or biological product for a rare pediatric disease may qualify for a voucher that can be redeemed to receive priority review for a different product. The sponsor may also transfer or sell the voucher to another sponsor. FDA awards rare pediatric disease priority review vouchers to sponsors of rare pediatric disease products that are approved and meet certain criteria, including a product candidate intended to treat a manifestation of a serious or life- threatening disease or condition in children aged 0 through 18 years of age. The rare pediatric disease priority review program began to sunset on December 20, 2024. The FDA may now only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for a drug and that designation was granted**

before December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers. There is no guarantee that any of our product candidates will be approved by that date, or at all. We may not obtain a priority review voucher prior to expiration of the program, unless Congress further reauthorizes the program. Our lead product candidates from our gene therapy platform, TN- 201 and TN- 401, have each been granted orphan drug designation by the FDA and the EC, and we may seek orphan drug designation for other product candidates in the U. S., Europe and other jurisdictions. ~~Even~~ **TN- 201 has also received rare pediatric disease designation from the FDA for MYBPC3- associated HCM. We may not be able to maintain orphan drug exclusivity for our product candidates and may not realize all the benefits of the orphan drug designation and the rare pediatric disease designation. Receiving these designations does not change FDA' s standards for regulatory approval of our product candidates and may not lead to faster regulatory review of any product candidate or increase the likelihood that any product candidate will receive marketing approval,** if **at all. We may seek orphan drug designation for other product candidates in the U. S., Europe and other jurisdictions, however, there can be no assurances that** we **will be able to** obtain orphan drug designation for ~~a~~ **our other** product ~~candidate~~ **candidates** ~~, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate and may not realize the benefits of such designation~~ . We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan- designated indication, in which case we could be precluded from receiving marketing approval for our product candidate for the applicable exclusivity period. In addition, exclusive marketing rights in the U. S. may be limited if we seek approval for an indication broader than the orphan- designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review. We may face difficulties from changes to current FDA and healthcare regulations and future legislation. Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U. S. or abroad. For example, certain policies of the current U. S. administration may impact our business and industry, which could impose significant burdens on, or otherwise materially delay, the FDA' s ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how current and future legislation, executive actions, and litigation, including the executive orders referenced below, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA' s and other agencies' ability to exercise their regulatory authority, including FDA' s pre- approval inspection and timely review of any regulatory filings or applications we submit to the FDA. If these executive actions impose constraints on FDA' s ability to engage in oversight and implementation activities in the normal course or constraints on our business operations, including operations of our contractors, our business may be negatively impacted. **In June 2024, the U. S. Supreme Court overruled the Chevron doctrine, which gives deference to regulatory agencies' statutory interpretations in litigation against federal government agencies, such as the FDA, where the law is ambiguous. This landmark Supreme Court decision may invite more companies and other stakeholders to bring lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, including FDA' s statutory interpretations of market exclusivities and the " substantial evidence " requirements for drug approvals, which could undermine the FDA' s authority, lead to uncertainties in the industry, and disrupt the FDA' s normal operations, any of which could delay the FDA' s review of our regulatory submissions. We cannot predict the full impact of this decision, future judicial challenges brought against the FDA, or the nature or extent of government regulation that may arise from future legislation or administrative action.** For example, in March 2010, ~~the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the~~ ACA ~~),~~ was passed, which substantially changed the way healthcare is financed by both the government and private insurers and continues to significantly impact the U. S. pharmaceutical industry. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, some of which have been successful, that create considerable uncertainty for our business. Although the U. S. Supreme Court held in 2021 that Texas and other challengers had no legal standing to challenge the ACA, we cannot predict how future challenges will impact our business, or what other healthcare measures and regulations **, including those directed at pricing and reimbursement,** will ultimately be implemented at the federal or state level or the effect of any future legislation or regulation may have on our business ~~. In addition, other legislative changes have been proposed and adopted in the U. S. since the ACA was enacted, including aggregate reductions to Medicare payments to providers, effective April 1, 2013, which, through subsequent amendments, will remain in effect through 2032 and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These and future laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations. Moreover, there has been heightened governmental scrutiny recently over~~

~~the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products~~ . Under the American Rescue Plan Act of 2021, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs was eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In ~~July 2021, the Biden administration released an executive order, " Promoting Competition in the American Economy, " with multiple provisions aimed at increasing competition for prescription drugs. In~~ August 2022, Congress passed the ~~Inflation Reduction Act of 2022 (the~~ IRA ~~)~~, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high- priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes. Various stakeholders, including pharmaceutical companies and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the IRA are unconstitutional. The impact of these judicial challenges **as well as future judicial challenges in view of the Supreme Court' s overturn of the Chevron doctrine** , legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the ~~government~~ **Trump administration** on us and the pharmaceutical industry as a whole is unclear **. Further, changes to the leadership of federal agencies under the new Trump administration, as well as new policies, executive orders and actions, such as a freeze on hiring, return- to- office policy, and a freeze on implementing new regulations and on external communications, may impact normal operations of the FDA and other agencies or result in a material impact on our clinical development plans and timelines** . The implementation of cost containment measures, including the prescription drug provisions under the IRA, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. We are unable to predict the future course of federal or state healthcare legislation in the U. S. directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations. We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. We are subject to stringent laws, rules, regulations, policies, industry standards and contractual obligations regarding data privacy and security and may be subject to additional related laws and regulations in jurisdictions into which we expand. Many of these laws and regulations are subject to change and reinterpretation and could result in claims, changes to our business practices, monetary penalties, increased cost of operations or other harm to our business. The regulatory framework for privacy and personal information security issues worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. The U. S. federal and various state, local and foreign government bodies and agencies have adopted or are considering adopting laws, rules, regulations and standards limiting, or laws, rules, regulations and standards regarding, the collection, distribution, use, disclosure, storage, security and other processing of personal information. Outside of the U. S., relevant legal requirements continue to evolve. For example, the collection and use of health data and other personal data including personal data collected in clinical trials is governed in the EU by the **General Data Protection Regulation (** GDPR **)** , which imposes substantial obligations upon companies and new rights for individuals, by certain EU member state- level legislation. The GDPR also forms part of the law of England and Wales, Scotland and Northern Ireland by virtue of section 3 of the European Union (Withdrawal) Act 2018 and as amended by the Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019 (SI 2019 / 419), known as UK GDPR. Failure to comply with the GDPR or UK GDPR may result in fines up to € 20, 000, 000 **(£ 17. 5 million in the UK)** or 4 % of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties. The GDPR or UK GDPR have increased our responsibility and liability in relation to personal data that we may process, and we may be required to implement additional measures in an effort to comply with the GDPR and UK GDPR or with other laws, rules, regulations and standards in the ~~European Economic Area (~~ EEA ~~)~~, ~~United Kingdom (~~ UK ~~)~~ and Switzerland relating to privacy and data protection. This may be onerous and if our efforts to comply with GDPR and UK

GDPR or other applicable laws, rules, regulations and standards are not successful, or are perceived to be unsuccessful, it could adversely affect our business. Further, restrictions on the transfer of personal data from the EEA, UK ~~and~~ **,** Switzerland **or other regions** to the U. S., ~~all of which~~ could restrict our activities in those jurisdictions, limit our ability to provide our products and services in those jurisdictions, require us to modify our policies and practices, and to engage in additional contractual negotiations, or increase our costs and obligations and impose limitations upon our ability to efficiently transfer personal data ~~from the EEA and Switzerland~~ to the U. S. In Canada, the Personal Information Protection and Electronic Documents Act (PIPEDA) and similar provincial laws impose obligations on companies with respect to processing personal information, including health- related information, regarding Canadian data subjects and provides individuals certain rights with respect to such information, including the right to access and challenge the accuracy of their personal information held by an organization. Failure to comply with PIPEDA, where applicable, could result in fines and penalties. In the U. S., a variety of data privacy, protection and security laws, rules, regulations and standards potentially may apply to our activities, such as state data breach notification laws, state personal data privacy laws ~~(~~**,** for example, the CCPA, state health information privacy laws, and federal and state consumer protection laws. The CCPA requires covered businesses that process personal information of California residents to disclose their data collection, use, sharing and retention practices, provides California residents with data privacy rights (including the ability to opt out of certain disclosures of personal information including for certain advertising purposes), imposes operational requirements for covered businesses, provides for significant civil penalties for violations as well as a private right of action for certain data breaches and statutory damages (that is expected to increase data breach class action litigation and result in significant exposure to costly legal judgments and settlements). Although there are limited exemptions for clinical trial data under the CCPA and certain other state laws, the CCPA and other new and evolving state laws could impact our business activities, depending on their interpretation. Numerous other states have enacted laws ~~similar~~ **relating** to ~~the CCPA~~ **privacy and data security that** either **are** in operation or slated to go into operation over the next ~~three~~ **several** years **. In many cases** , **these laws** ~~and other state legislatures~~ are ~~considering and may adopt their own~~ comprehensive ~~data~~ privacy ~~and security~~ laws **similar to the CCPA** , with potentially greater penalties and more rigorous compliance requirements **. States also are enacting laws addressing specific subject matter, such as Washington' s My Health, My Data Act, which includes a private right of action** . Laws in all 50 states may require businesses to provide notice to individuals whose personal data has been disclosed as a result of a data breach. Finally, federal, state and foreign laws, rules, regulations and standards may apply generally to the privacy and security of information we maintain, and may differ from each other significantly, thus complicating compliance efforts and potentially requiring us to undertake additional measures to comply with them. With the GDPR, PIPEDA, CCPA, and other laws, regulations and other obligations relating to privacy and data protection imposing new and relatively burdensome obligations, and with substantial uncertainty over the interpretation and application of these and other obligations, we may face challenges in addressing their requirements and making necessary changes to our policies and practices and may incur significant costs and expenses in an effort to do so. We make public statements about our use, collection, disclosure and other processing of personal data through our privacy policies, information provided on our website and press statements. Although we endeavor to comply with our public statements and documentation, we may at times fail to do so or be alleged to have failed to do so. Any failure or perceived failure by us or our vendors or service providers to comply with our applicable policies or notices relating to privacy or data protection, our contractual or other obligations to third parties, or any of our other legal obligations, laws, rules, regulations and standards relating to privacy or data protection, may result in governmental investigations or enforcement actions, litigation, claims and other proceedings, harm our reputation, and could result in significant liability. Our relationships with healthcare professionals, clinical investigators, CROs and third- party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, which could expose us to significant losses, including, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings. Healthcare providers and third- party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, as well as market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations may include the following: • the federal Anti-Kickback Statute which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid; • the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; • the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; • the Civil Monetary Penalty Act of 1981 and implementing regulations, which impose penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent, or offered or transferred remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary' s decision to order or receive items or

services reimbursable by the government from a particular provider or supplier; • the HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their implementing regulations, also imposes obligations, including mandatory contractual terms, on covered entities, which are health plans, healthcare clearinghouses, and certain health care providers, as those terms are defined by HIPAA, and their respective business associates and their subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; • the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program, with specific exceptions, to annually report to CMS information regarding payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician healthcare professionals (such as nurse practitioners and physician assistants, among others), and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members; and • analogous state and foreign laws and regulations, such as state anti- kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance regulations promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; state and local laws that require the registration of pharmaceutical sales and medical representatives; state laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare and data privacy and security laws and regulations will involve substantial ongoing costs and may require us to undertake or implement additional policies or measures. We may face claims and proceedings by private parties, and claims, investigations and other proceedings by governmental authorities, relating to allegations that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations, and it is possible that courts or governmental authorities may conclude that we have not complied with them, or that we may find it necessary or appropriate to settle any such claims or other proceedings. In connection with any such claims, proceedings, or settlements, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time- consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CDMOs, suppliers and vendors may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements. We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CDMOs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, 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. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter misconduct by these 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 comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers'

compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of hazardous and flammable materials, including chemicals and biological materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. Our business activities are subject to the U. S. Foreign Corrupt Practices Act and similar anti- bribery and anti- corruption laws of other countries in which we operate, as well as U. S. and certain foreign export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them. Our business activities are subject to the U. S. Foreign Corrupt Practices Act of 1977, as amended (FCPA), the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, and similar anti- bribery or anti- corruption laws, regulations or rules of other countries in which we operate. These laws generally prohibit companies and their employees and agents from offering or providing improper payments or benefits to recipients in the public or private sector. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non- U. S. governments. Additionally, in many other countries, hospitals are owned and operated by the government, and doctors and other hospital employees would be considered foreign officials under the FCPA. ~~Recently, the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies.~~ We sometimes leverage third parties to assist with the conduct of our business abroad. As we increase our international business activities, our risks under these laws may increase. We, our employees and agents may have direct or indirect interactions with officials and employees of government agencies or state- owned or affiliated entities and may be held liable for the corrupt or other illegal activities of these employees and agents even if we do not explicitly authorize such activities. These laws also require that we make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls and compliance procedures designed to prevent violations of anti- corruption laws. While we have policies and procedures to address compliance with such laws, we cannot assure you that all of our employees and agents will not take actions in violation of applicable law for which we may be ultimately held responsible. Allegations or violations of these laws and regulations could result in whistleblower complaints, fines, severe civil or criminal sanctions, settlements, prosecution, enforcement actions, damages, adverse media coverage, investigations, loss of export privileges, disgorgement, and other remedial measures, suspension or debarment from government contracts and prohibitions on the conduct of our business including our ability to offer our products in one or more countries. Responding to any investigation or action will likely result in a materially significant diversion of management' s attention and resources and significant defense costs and other professional fees. As a general matter, investigations, enforcement actions and sanctions could damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition. In addition, our products may be subject to U. S. and foreign export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and / or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to, existing or potential customers with international operations. In particular, there is currently significant uncertainty about the future relationship between the United States and various other countries, ~~most significantly~~ **including, without limitation,** China **, Mexico and Canada** , with respect to trade policies, treaties, tariffs, taxes, and other limitations on cross- border operations. The U. S. government has made and continues to make significant additional changes in U. S. trade policy and may continue to take future actions that could negatively impact U. S. trade. For example, legislation has been introduced in Congress to limit certain U. S. biotechnology companies from using equipment or services produced or provided by select Chinese biotechnology companies, and others in Congress have advocated for the use of existing executive branch authorities to limit those Chinese service providers' ability to engage in business in the U. S. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to such actions or what actions may be taken by the other countries in retaliation. If we are unable to obtain or use services from existing service providers or become unable to export or sell our products to any of our customers or service providers, our business, liquidity, financial condition, and / or results of operations would be materially and adversely affected. Changes in tax law could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition. Changes in tax law, including to the orphan drug tax credit and other changes to U. S. and non- U. S. taxation, could increase our tax liability and adversely affect our operating results. For example, starting from January 1, 2022, the Tax Cuts and Jobs Act of 2017 requires taxpayers to capitalize domestic research and development costs in the year incurred and amortize such costs rather than deduct such costs in the year incurred. When and if we become profitable, these changes may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and may increase our total federal tax liability attributable to orphan drug programs and other research and development. In addition, the Inflation Reduction Act of 2022 imposes a 1 % excise tax on certain repurchases of stock made on or after January 1, 2023. These changes could increase our total federal tax liability when and if we become profitable. Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to Our Business Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees. We are highly dependent on the principal members of our management, our scientific founders and

other scientific and clinical advisors and consultants, and our scientific and medical staff. If we do not succeed in attracting and retaining such personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We do not maintain " key person " insurance for any of our executives or other employees. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high- quality candidates than what we have to offer. If we are unable to continue to attract and retain high- quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed. Additionally, we rely on our scientific founders and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non- compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with our scientific founders or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be significantly harmed. In order to successfully implement our long- term plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth. In order to successfully implement our development and commercialization plans and strategies, we expect to need additional managerial, operational, sales, marketing, financial and other personnel in the future. Our future financial performance and our ability to successfully develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day- to- day activities in order to devote a substantial amount of time to managing these growth activities. We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of our research and development, clinical development, manufacturing and operations. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third- party service providers is compromised for any reason, our preclinical studies and the initiation and conduct of our planned clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of our product candidates or otherwise advance our programs and business. We cannot assure you that we will be able to manage our existing third- party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all. If, subject to the successful clinical development of our product candidates, we are not able to effectively expand our organization by hiring new employees and / or engaging additional third- party service providers, we may not be able to successfully implement the tasks necessary to develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals. Our computer systems, or those of any of our CROs, manufacturers, contractors, consultants or other third parties or potential future collaborators, may fail or suffer security incidents or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations. As part of our business, we and our CROs, manufacturers, contractors (including sites performing our clinical trials), consultants and other third parties, collect, maintain and transmit sensitive data on our networks and systems, including our intellectual property and proprietary and confidential business information (such as research data and personal information). Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems, and those of our third- party CROs, manufacturers, contractors (including sites performing our clinical trials), consultants and other third parties, such systems are vulnerable to breakdown or other damage or interruption from, among other things, inadvertent or intentional actions by our employees, contractors, consultants, business partners, and other third parties ~~,~~ **and** cyber- attacks and other hacking attempts by malicious third parties, which may **disrupt or** compromise our system infrastructure or lead to the loss, destruction, alteration, prevention of access to, disclosure, dissemination of, or damage or unauthorized access to, our data or other data that we process or maintain or that is processed or maintained on our behalf, or other assets. Although we have not observed material impacts of cyber- attacks on our operations and financial condition to date, we and our third- party service providers have frequently been the target of threats of this nature and we expect these threats and attacks to continue. Any ~~data~~ **disruption or security** breach ~~,~~ ~~disruption~~ or ~~security~~ incident resulting in any loss, destruction, unavailability, alteration, disclosure ~~,~~ **or** dissemination of, or damage or unauthorized access to, our data, or any other data that we **maintain or otherwise** process ~~or maintain~~ or that is **maintained or otherwise** processed ~~or maintained~~ on our behalf, or other assets, or for it to be believed or reported that any of the foregoing occurred, could cause us to incur significant liability, including consequential damages, financial harm and reputational damage and the development and commercialization of our product candidates could be delayed. The loss, corruption, or unavailability of clinical trial data for our product candidates also could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. We cannot ensure that our data protection **or cybersecurity** efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other

third parties, will prevent breakdowns in our or their systems or have prevented, or will prevent, ~~cybersecurity~~ ----- **security** breaches or incidents, including those that cause loss, destruction, unavailability, alteration, dissemination of, or damage or unauthorized access to, our data, including personal data, **or other** assets ~~and or~~ other data processed or maintained on our behalf. Any such breakdowns, breaches, or incidents, and any resulting impacts, could have a material adverse effect upon our reputation, business, operations ~~or~~ **and** financial condition. We also rely on third parties to support the development and manufacture of our product candidates, and any ~~data~~ **security** breaches **or other incidents** or other security events relating to their computer systems could also have a material adverse effect on our business. Controls employed by our information technology department and our CROs, consultants and other third parties could prove inadequate, and our ability to monitor such third parties' ~~data security~~ **cybersecurity** practices is limited. Due to applicable laws, rules, regulations and standards or contractual obligations, we may be held responsible for any ~~information security failure or~~ cyber- attack **, security breach or incident or cybersecurity failure** attributed to our third- party service providers as **relevant to the information** they **maintain or otherwise process for us** ~~relate to the information we share with them~~ . We maintain limited cybersecurity insurance and therefore the successful assertion of one or more large claims against us in connection with a breach or other cybersecurity- related matter could adversely affect our business, financial condition, results of operations and prospects. Notifications and follow- up actions related to a data breach or other security incident could impact our reputation and cause us to incur significant costs, including significant legal expenses and remediation costs. We expect to incur significant costs in an effort to detect and prevent security **breaches and other** incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security **breach or other** incident. However, we cannot guarantee that we will be able to detect or prevent any such **breaches or** incidents, or that we can identify, remediate or otherwise address any such **breaches or** incidents in an effective or timely manner. Our efforts to improve security and protect data from compromise may also identify previously undiscovered instances of data breaches or other cybersecurity incidents. Any ~~data~~ **disruption or security** breach ~~, disruption~~ or ~~security~~ incident resulting in any loss, destruction, or alteration of, **or** damage, unauthorized access to or inappropriate or unauthorized disclosure **,** ~~of or~~ dissemination **or other processing** of, our data, including personal data, or other information ~~that is~~ **maintained or otherwise** processed ~~or maintained~~ on our behalf, or ~~if~~ any **belief or reporting of any** of these **matters having** ~~is believed or reported to have~~ occurred, ~~we~~ could ~~be exposed~~ - **expose us** to litigation and governmental investigations and inquiries, **could lead to delays in** the further development and commercialization of our product candidates **, and** could **result in** ~~be delayed, and we could be subject to~~ significant fines or penalties for any noncompliance with certain state, federal and international privacy and security laws, rules, regulations and standards. Our operations are vulnerable to interruption by fire, earthquakes, power loss, telecommunications failure, terrorist activity, pandemics and other events beyond our control, which could harm our business. Our facilities are located in the San Francisco Bay Area. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major earthquake, flood, blizzard, wildfire, power loss, terrorist activity, pandemics or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. Also, our CDMOs and suppliers' facilities are located in multiple locations where other natural disasters or similar events which could severely disrupt our operations, could expose us to liability and could have a material adverse effect on our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. A variety of risks associated with development and marketing our product candidates internationally, subject to regulatory approval in applicable jurisdictions, could materially adversely affect our business. We may seek regulatory approval of our product candidates outside of the U. S. and / or work with contractors or partners in foreign jurisdictions, and we expect that we will be subject to additional risks and requirements related to our operations in foreign countries, including: • differing regulatory requirements and reimbursement regimes; • unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements; • economic weakness, including inflation, or political instability in particular foreign economies and markets; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • foreign taxes, including withholding of payroll taxes; • foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; • difficulties staffing and managing foreign operations; • workforce uncertainty in countries where labor unrest is more common than in the U. S.; • potential liability under the FCPA or comparable foreign regulations; • challenges obtaining, maintaining, protecting, defending and enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the U. S.; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from geo- political actions, including war and terrorism ~~, including effects of the Russia- Ukraine and Middle East conflicts~~ . These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations. Risks Related to Our Intellectual Property Our commercial success depends in large part on our ability to obtain, maintain, protect, defend and enforce patents, trade secrets and other intellectual property relating to our product candidates and platforms and to operate without infringing, misappropriating or otherwise violating the intellectual property of others. We rely on patent, copyright, trade secret and trademark laws in the U. S. and certain other countries to protect our technology, and we generally seek to protect our position by filing patent applications in the U. S. and abroad and by acquiring or in- licensing relevant issued patents or pending applications from third parties. However, these efforts may provide only limited protection. There can be no assurance that we or our licensors will obtain any additional issued patents or that any issued patents we or our licensors obtain will provide us with any competitive advantage. Pending patent applications cannot be enforced until issued, and then only to the extent the issued claims cover the product candidate or relevant technology. There can be no assurance that our patent applications or the patent applications of our licensors will result in additional patents being issued or that any such

issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable, or they may be modified, narrowed in scope, or revoked in proceedings instituted by third parties before various patent offices or in courts in the U. S. and abroad. The degree of future protection for our and our licensor' s intellectual property and 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. These uncertainties and limitations in our ability to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations. Any failure to obtain or maintain patent protection with respect to our technology and product candidates would have a material adverse effect on our business, financial condition, results of operations and prospects. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future licensors or collaborators will be successful in protecting our product candidates and platforms by obtaining and defending adequate patent coverage. These risks and uncertainties include the following: • the **United States Patent and Trademark Office (** USPTO **)** and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the non- compliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction; • patent applications may not result in any patents being issued; • patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, narrowed in scope or otherwise may not provide any competitive advantage; • our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates; • there may be significant pressure on the U. S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and • countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates and limiting the scope of our protection in countries outside the United States. The patent prosecution process is also expensive and time- consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. We may be unable to obtain or maintain patent applications and patents due to the subject matter claimed in such patent applications and patents being in disclosures in the public domain. It is also possible that we or our licensors will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Furthermore, although we enter into non- disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third- party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected. The patent position of biotechnology companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of our licensors may not result in patents being issued which protect our product candidates and platforms or which effectively prevent others from commercializing competitive product candidates and technologies or otherwise provide any commercial advantage. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own or in- license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Our competitors or other third parties may avail themselves of safe harbor under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch- Waxman Amendments) to conduct research and clinical trials and may be able to circumvent our patent rights by developing similar or alternative technologies or products in a non- infringing manner. Any patents that we may own or in- license may be challenged or circumvented by third parties or may be narrowed, rendered unenforceable, or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable or remain protected by valid and enforceable patents. While we believe our intellectual property allows us to pursue our current development programs, we may not be aware of all third- party intellectual property rights potentially relating to our technology and product candidates. We cannot be certain that we were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and the inventorship, scope, validity or enforceability of our **patents,** potential future patents or the patents of our licensors that may be challenged in the courts or patent offices in the U. S. and abroad. For example, we may be subject to a third- party pre- issuance submission of prior art, post- grant review or inter partes review at the USPTO, or other

similar proceedings including, opposition, derivation, revocation or reexamination proceedings in the U. S. or abroad. A third party may also claim that our patents or licensed patent rights are invalid or unenforceable in a litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our **patents,** potential future ~~owned~~ patents or licensed patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us. Such proceedings also may result in substantial cost and require significant time from our scientists, manufacturing staff and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our **patents,** potential future patents and patent applications or the patents and patent applications of our licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize our product candidates. Our research, development and commercialization activities may be subject to claims that we infringe, misappropriate or otherwise violate patents or other intellectual property rights of others. Additionally, other entities may have, develop or obtain patents that could impair our competitive position or limit our ability to make, use, sell, offer for sale or import our product candidates. There is a substantial amount of litigation, both within and outside the U. S., involving patent and other intellectual property rights in the biotechnology industry. Numerous third- party U. S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. Third- party patents or patent applications may include claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Given the vast number of patents in our field of technology, we cannot be certain or guarantee that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. For example, we are aware of third- party patent rights that could be construed to cover the use of our TN- 201 product candidate. We believe that if these third- party patent rights were to be asserted against us, we would have valid defenses against such assertions, including that such patent rights are invalid and / or not infringed. However, if such third- party patent rights were asserted against us and found to be valid, enforceable and infringed, we could be liable for damages and be required to obtain a license to such patent rights prior to commercializing TN- 201 both within and outside the U. S., and such license may not be available on commercially reasonable terms or at all. Additionally, we are aware of third- party patent rights related to the use of certain AAV vectors, which have been asserted against others, including in at least one instance against a company for pre- approval activities. If these patent rights were to be asserted against us, we believe we would have valid defenses against such assertions, including that such patent rights are invalid and / or not infringed. However, such defenses may not be successful and we could be liable for damages and need to secure a license to such patent rights, which may not be available on commercially reasonable terms or at all. In the event any of the foregoing were to occur, we may be prevented from further developing and commercializing any affected product candidates, including TN- 201. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement, misappropriation or other violation of the patent or other intellectual property rights of third parties. Although no third party has asserted a claim of patent infringement against us as of the date of this periodic report, there can be no assurance that we will not be subject to claims of patent or other intellectual property infringement in the future. Furthermore, we may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. We may incorrectly conclude that a third- party patent is invalid, unenforceable or not infringed by our activities. Pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technology and product candidates. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third- party patents that may be infringed by commercialization of any 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. 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 ambiguity in the meaning of patent claims. **Generative artificial intelligence (AI) resources that are publicly available also present a risk that a company may inadvertently obtain, incorporate or use a third party' s intellectual property.** Third parties may assert patent infringement claims against us directed at any of our product candidates based on ~~our~~ existing patent applications or patents that may be granted in the future, regardless of their merit. Any patent- related legal action against us claiming damages and seeking to enjoin commercial activities relating to our products, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates. Defense of these claims would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. Because of the inevitable uncertainty in intellectual property litigation, we could lose a patent infringement or other action asserted against us regardless of our perception of the merits of the case. 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 and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Patent and other types of intellectual property litigation can involve complex

factual and legal questions, and their outcome is uncertain. There is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any future products we may develop and any other future products or technologies covered by the asserted third- party patents. In order to successfully challenge the validity of any such U. S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U. S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U. S. patent or find that our technology did not infringe any such claims. Further, even if we were successful in defending against any such claims, such claims could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. We may in the future pursue invalidity proceedings with respect to third- party patents. The outcome following legal assertions of invalidity is unpredictable. Even if resolved in our favor, these legal proceedings 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 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 proceedings adequately. Some of these third parties may be able to sustain the costs of such proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent proceedings could compromise our ability to compete in the marketplace. If we do not prevail in the patent proceedings the third parties may assert a claim of patent infringement directed at our product candidates. In addition, our agreements with some of our suppliers or other entities with whom we do business require us to defend or indemnify these parties to the extent they become involved in infringement claims, including the types of claims described above. We could also voluntarily agree to defend or indemnify third parties in instances where we are not obligated to do so if we determine it would be important to our business relationships. If we are required or agree to defend or indemnify third parties in connection with any infringement claims, we could incur significant costs and expenses that could adversely affect our business, operating results or financial condition. We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in- licenses. Many pharmaceutical companies, biotechnology companies, and academic institutions may have patents and patent applications potentially relevant to our business. We may find it necessary or prudent to obtain licenses to such patents from such third- party intellectual property holders, for example, in order to avoid infringing these third-party patents. We may also require licenses from third parties for certain technologies for use with our product candidates. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third- party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also expect that competition for the in- licensing or acquisition of third- party intellectual property rights that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. We 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 or at all. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Changes in U. S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. Changes in either the patent laws or in the interpretations of patent laws in the U. S. and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our **patents,** potential future patents or in third- party patents. In addition, the U. S. Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Furthermore, the U. S. Supreme Court and the U. S. Court of Appeals for the Federal Circuit have made, and will likely continue to make, changes in how patent laws in the U. S. are interpreted. The U. S. 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. **For example, the U. S. Supreme Court held in Amgen v. Sanofi (2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. In addition, the U. S. Court of Appeals for the Federal Circuit recently issued a decision involving the interaction of a patent term adjustment, terminal disclaimers, and obvious- type double patenting. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained.** Similarly, foreign courts have made and will continue to make changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by U. S. and foreign legislative bodies. **For example, the IRA passed by Congress authorizes the Secretary of the Department of HHS to negotiate prices directly with participating manufacturers for selected medicines covered by Medicare even if these medicines are protected by an existing patent. While we do not believe that the IRA or its effects will impact our ability to obtain patents in the near future, we cannot be certain**

whether it will affect our patent strategy in the long run. 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 patent and the patents we might obtain or license in the future. We may be subject to claims challenging the inventorship or ownership of our owned **patents,** patent applications or in- licensed patent rights and other intellectual property. We or our licensors may be subject to claims that former employees or other third parties have an ownership interest in our owned **patents,** patent applications or in-licensed patents, trade secrets or other intellectual property rights as an inventor or co- inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or other third parties who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our **patents,** patent applications or our licensors' owned or in- licensed patents, trade secrets or other intellectual property rights. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property rights that are important to our product candidates. It may be necessary or we may desire to enter into a license to settle any such claim; however, there can be no assurance that we would be able to obtain a license on commercially reasonable terms, if at all. 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 distraction to management and other employees, and any litigation or the threat of litigation may adversely impact our reputation or affect our ability to hire employees or contract with independent contractors. In addition, while it is our policy to require our employees, consultants, advisors, contractors and other third parties who may be involved in the conception or development of intellectual property rights to execute agreements assigning such intellectual property rights to us, we or our licensors may be unsuccessful in executing such agreements with each party who, in fact, conceives or develops intellectual property rights that we regard as our own. The assignment of intellectual property rights may not be self- executing or sufficient in scope, or the assignment agreements may be breached, and we or our licensors may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property rights. Furthermore, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us or our licensors may be ineffective in perfecting ownership of inventions developed by that individual. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects. Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. 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. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If we do not obtain patent term extension for our product candidates, our business may be materially harmed. Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U. S. patents or those of our licensors may be eligible for limited patent term restoration under the Hatch- Waxman Amendments. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. We may not be granted any extensions for which we apply in the U. S. or any other jurisdiction because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in- license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or restoration, or the foreign equivalent, or if the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents 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., even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the U. S., even in jurisdictions where we or our licensors do pursue patent protection. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own competing 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. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. European patent applications now have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unified Patent Court (UPC). This is a significant change in European patent practice. As the UPC is a relatively new court system, there is limited precedent for the court, increasing the uncertainty of any litigation. As a single court system can invalidate a European patent, we, where applicable, have opted out of the UPC and as such, but for proceedings such as an opposition, each European patent would need to be challenged in each individual country. Geo- political actions in the U. S. and in foreign countries could

increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. Government actions may also prevent filing, prosecution and maintenance of issued patents in various jurisdictions. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in such jurisdictions. If such an event were to occur, it could have a material adverse effect on our business. In addition, jurisdictions outside of the U. S. could also permit our patents to be exploited without consent or compensation. In such circumstances we would not be able to prevent third parties from practicing our inventions or from selling or importing products made using our inventions in and into such jurisdictions. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or patent applications will be due to the USPTO and various foreign patent offices outside of the U. S. at various points over the lifetime of our **current,** potential future patents and patent applications and those of our licensors. We rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. An inadvertent lapse or non- compliance with such requirements can sometimes be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business, financial condition and results of operations. 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. We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products, but we do not yet own a U. S. registered trademark for our corporate name, " Tenaya ". Once filed and registered, our potential future 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 potential future 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. As a means to enforce our potential future trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings, which can be expensive and time-consuming. 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 potential future 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. Additionally, our potential future registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our potential future trademark applications and registrations, and our potential future trademarks may not survive such proceedings. If we do not secure registrations for our potential future trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would. Our efforts to enforce or protect our proprietary rights related to trademarks, domain names or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patent protection on the intellectual property underlying our technology and product candidates, we also rely on the protection of our trade secrets, including unpatented know- how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know- how, including entering into confidentiality agreements with third parties who have access to such information, and confidential information and invention assignment agreements with employees, consultants, advisors and other third parties involved in the development of intellectual property, we cannot guarantee that we and our licensors have entered into such agreements with each party that may have had access to our trade secrets or proprietary information or that has been involved in the development of intellectual property. Additionally, we cannot provide any assurances that all such agreements have been duly executed, that these parties will not breach such agreements and disclose our proprietary information, including our trade secrets, or that we would be able to obtain adequate remedies for such breaches should they occur. We may not be able to prevent the unauthorized disclosure or use of our trade secrets. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U. S. are less willing or unwilling to protect trade secrets. Given that our proprietary position is based, in part, on our know- how and trade secrets and despite our efforts to protect our trade secrets, our competitors' discovery of our proprietary technology, trade secrets or confidential information or other unauthorized use or disclosure of such information would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, third parties may still derive similar information independently, and we would have no right to prevent

them from using that information to compete with us. We expect know- how and information to be disseminated over time within the industry through independent development, publication of journal articles, and movement of personnel between companies and from academic to industry scientific positions. We seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems, but such security measures may be breached, and we may not have adequate remedies for any such breach. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. We may be subject to claims that we or our employees, consultants, advisors or contractors have wrongfully used or disclosed alleged confidential information or trade secrets. 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 these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology and pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or consultants inadvertently or otherwise used or disclosed trade secrets or confidential or other information proprietary of their former employers or their former or current clients. In addition, we have entered into and may in the future enter into non- disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as collaborators, CROs, third- party manufacturers, consultants, potential partners and other third parties. We may become subject to litigation where a third party asserts that we or our employees or other third parties inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. Defense of any such claims, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of resources from our business. We cannot predict whether we would prevail in any such claims. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, including the loss of valuable intellectual property rights or personnel, all of which could adversely affect 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 and other employees. Our rights to develop and commercialize our technology and product candidates may be subject, in part, to us obtaining licenses from others and the terms and conditions of such licenses. If we fail to comply with our obligations in any agreement under which we license intellectual property rights from third parties, we could lose licensed rights that are important to our business. We have entered into and may in the future enter into additional license agreements with third parties to advance our research or allow commercialization of product candidates. These licenses may not provide us with exclusive rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products. In addition, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license. If our licensors fail to prosecute, maintain, enforce, and defend, or lose rights to such patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any product that is the subject of such licensed rights could be adversely affected. Even where we have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions taken by or on behalf of our licensors prior to the date upon which we assumed control over patent prosecution. Our licensors may have relied on third- party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in- licensed. If other third parties have ownership rights to our in- licensed patents, our rights to use the licensed intellectual property would not be exclusive and they may be able to license such patents to our competitors, permitting our competitors to market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. For example, the intellectual property we ~~license~~ **licensed** from the University of Texas, Southwestern (UTSW) is subject to certain non- commercial rights reserved by UTSW. Patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against our licensors or another licensee or in administrative proceedings brought by or against our licensors or another licensee in response to such litigation or for other reasons. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products, including in territories covered by our licenses. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. Our current licenses impose, and our future licenses likely will impose, various diligence, royalty payment, milestone payment, insurance and other obligations on us. If we fail to comply with any of these or other obligations in our license agreements, we may be required to pay damages and the licensor may have the right to terminate the licenses. Termination by the licensor would cause us to lose valuable rights and could prevent us from developing and commercializing our product candidates and proprietary technologies. Our business would be seriously harmed if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. If any such event occurs, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Further, we may have to negotiate new or reinstated licenses with less favorable terms or we may not have sufficient intellectual property rights to operate our business.

This could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects. The agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. Disputes may arise between us and our current and future licensors. In spite of our efforts, our current and future licensors might conclude that we have materially breached our obligations under our license agreements and might therefore terminate such license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, or are insufficient to provide us the necessary rights to use the intellectual property rights, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. Our licensors may also own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating our licensor' s rights. In addition, while we cannot currently determine the amount of royalty obligations we would be required to pay on the sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in product candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize any product candidates, we may be unable to achieve or maintain profitability. Intellectual property discovered through government funded programs 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. We have in- licensed, and we may develop, acquire or in- license in the future, certain patents, patent applications or other intellectual property generated using U. S. government funding or grants. Pursuant to the Bayh- Dole Act of 1980, the U. S. government has certain rights in inventions developed with government funding. These rights 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, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non- exclusive licenses to any of these inventions to a third- party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as march- in rights). If the U. S. government exercises its march- in rights in our current or future intellectual property rights generated using U. S. government funding or grants, we could be forced to license or sublicense intellectual property developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U. S. government for the exercise of such rights. The U. S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. 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 any of these inventions or produced through the use of any of these inventions be manufactured substantially in the U. S. This preference for U. S. industry may limit our ability to contract with non- U. S. product manufacturers for products covered by such intellectual property, and may be waived by the federal agency that provided the funding if the owner or assignee 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. Any failure by us to comply with federal regulations regarding intellectual property rights that were developed through the use of U. S. government funding could have a material adverse effect on our business, financial condition, results of operations, and prospects. Risks Related to Our Dependence on Third Parties The third parties upon which we rely to conduct our preclinical studies and clinical trials have a significant role in the conduct of such drug development activities and the subsequent collection and analysis of data. These third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we have limited ability to control the amount or timing of resources that any such third party devotes to our preclinical studies or our clinical trials. The third parties we rely on for these services may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. Some of these third parties may terminate their engagements with us at any time. We also expect to have to negotiate budgets and contracts with CROs and clinical trial sites and we may not be able to do so on favorable terms. If we need to enter into alternative arrangements with, or replace or add any third parties, it would involve a transition period, and may require substantial cost and extensive management time and focus. Any of these events may delay our drug development activities, increase costs, and materially impact our ability to meet our desired clinical development timelines. Our heavy reliance on these third parties for such drug development activities reduces our control over these activities. As a result, we have less direct control over the conduct, timing and completion of preclinical studies and clinical trials and the management of data developed through such drug development activities than if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, such as GCP and cGMP, and our reliance on third parties does not relieve us of these responsibilities. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable requirements, such as GCP or cGMP, the

clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials substantially comply with applicable regulations. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able, or may be delayed in, obtaining marketing approvals for our product candidates or otherwise successfully commercializing our product candidates. We rely on third parties to produce **and maintain** certain of our product candidates. This increases the risk that we will not have sufficient quality and quantities of product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our business. We do not have long- term supply agreements, and we purchase our required drug product on a purchase order basis, which means that aside from any binding purchase orders we may have, our supplier could cease supplying to us or change the terms on which it is willing to continue supplying to us at any time. If we experience an unexpected loss of supply of our product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing preclinical studies or clinical trials. Furthermore, any decision by us to change a third- party manufacturer could result in delays in our manufacturing supply chain which could delay or otherwise impact development of our programs and result in increased costs. We may be unable to maintain or establish required agreements with third- party manufacturers on acceptable terms. Even if we are able to do so, reliance on third- party manufacturers entails additional risks, including: • the failure of the third party to manufacture our product candidates according to our schedule and specifications, or at all, including if our third- party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them; • the termination or nonrenewal of arrangements or agreements by our third- party contractors at a time that is costly or inconvenient for us; • the breach by the third- party contractors of our agreements with them; • the failure of third- party contractors to manufacture our product candidates according to our specifications or comply with applicable regulatory requirements, including cGMP; • the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified; • clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and • the infringement, misappropriation or other violation of our intellectual property or proprietary information. We do not have complete control over all aspects of the manufacturing process of our CDMOs and are dependent on these CDMOs for compliance with cGMP regulations for manufacturing API, drug substance and finished drug products. We are in the process of developing our supply chain for ~~each~~ **certain** of our product candidates and intend to put in place framework agreements under which CDMOs will provide us with necessary quantities of API, drug substance and drug product based on our development needs. As we advance our product candidates through development, we will consider our lack of redundant supply for each of our product candidates to protect against any potential supply disruptions. However, we may be unsuccessful in putting in place such framework agreements or protecting against potential supply disruptions. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations. We rely on third- party suppliers for the raw materials required for the production of our product candidates for all of our programs. Our dependence on these third- party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors who are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would seriously harm our business. Our dependence upon others for the manufacture **and ongoing storage and ongoing testing** of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis. If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks. From time to time, we evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including: • increased operating expenses and cash requirements; • the assumption of additional indebtedness or contingent liabilities; • the issuance of our equity securities; • assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel; • the diversion of our management' s attention from our existing programs and initiatives in pursuing such a strategic partnership or acquisition; • unauthorized use or disclosure of our confidential information accessed in connection with partnership activities; • the loss of key personnel and uncertainties in our ability to maintain key business relationships; • risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; • our inability to generate revenue from acquired technology and / or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs; and • our inability to realize anticipated efficiencies and strategic benefits from such acquisitions or strategic partnerships. In addition, if we

undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one- time expenses and acquire intangible assets that could result in significant future amortization expense. We may enter into collaborations with third parties for the development and commercialization of product candidates. If we are not able to establish those collaborations on commercially reasonable terms or those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates. We strategically evaluate collaborations and partnerships with biopharmaceutical companies that may have more robust and complementary capabilities and resources to accelerate the development and maximize the availability and potential of our product candidates. The collaboration negotiation process is time- consuming and complex. If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors regarding our business, the applicable product candidate or technology subject to the collaboration negotiation and the related market potential. If we are unable to reach a definitive agreement, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. If we enter into any collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates would pose numerous risks to us, including the following: • collaborators have significant discretion in determining the efforts and resources that they will apply to, and the manner in which they perform their obligations under, these collaborations and may not perform their obligations as expected; • the relationship 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; • collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a business combination or sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; • a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products; • we may grant exclusive rights to our collaborators that would prevent us from collaborating with others; • collaborators may not properly obtain, maintain, defend, protect or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property- related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings; • disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; • collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all; • collaborators may not provide us with timely and accurate information regarding development progress and activities under the collaboration or may limit our ability to share such information, which could adversely impact our ability to report progress to our investors and otherwise plan our own development of our product candidates; • collaborators may own or co- own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and • a collaborator' s sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings. If an agreement with a collaborator terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator' s technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this " Risk Factors " section, and any negative impact on our collaborators may adversely affect us. If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved. We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. There are risks involved

with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel. If we enter into arrangements with third parties to perform sales, marketing, commercial support and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved and our business would be seriously harmed. Risks Related to the Securities Market and Ownership of Our Common Stock The price of our stock is volatile, and you could lose all or part of your investment. The trading price of our common stock is highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this " Risk Factors " section and elsewhere in this periodic report, these factors include: • the timing of achievement of our research, clinical, regulatory and other milestones for our product candidates; • the results of preclinical studies and clinical trials of our product candidates, those conducted by third parties or those of our competitors; • the success of competitive products or announcements by potential competitors of their product development efforts; • regulatory actions with respect to our product candidates or those of our competitors; • actual or anticipated changes in our growth rate relative to our competitors; • regulatory or legal developments in the U. S. and other countries; • litigation, including developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights; • the recruitment or departure of key personnel; • announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments; • actual or anticipated changes in estimates as to financial results, development timelines or coverage and / or recommendations by securities analysts; • fluctuations in the valuation of companies perceived by investors to be comparable to us; • market conditions in the pharmaceutical and biotechnology sector; • changes in the structure of healthcare payment systems; • share price and volume fluctuations attributable to inconsistent trading volume levels of our shares; • announcement or expectation of additional financing efforts; • sales of our common stock by us, our insiders or our other stockholders; • expiration of market stand- off or lock- up agreements; • the impact of any natural disasters or public health emergencies, such as the COVID- 19 pandemic; • fluctuations in interest rates and inflation rates; and • general economic, political, industry and market conditions. The realization of any of the above risks or any of a broad range of other risks, including those described in this " Risk Factors " section, could have a dramatic and adverse impact on the market price of our common stock. **If we fail to maintain compliance with the minimum listing requirements, our common stock will be subject to delisting. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if our common stock is delisted. The continued listing standards of the Nasdaq Global Select Market (Nasdaq) require, among other things, that the minimum price of a listed company' s stock be at or above $ 1. 00. If the minimum bid price is below $ 1. 00 for a period of more than 30 consecutive trading days, the listed company will fail to be in compliance with Nasdaq' s listing rules and, if it does not regain compliance within the 180- day grace period, will be subject to delisting. If the bid price of our common stock closes below the minimum $ 1. 00 per share requirement and we fail to regain compliance prior to the expiration of the initial 30 consecutive trading days, we would expect to receive a notification of noncompliance from Nasdaq. In accordance with Nasdaq' s listing rules, we would expect to be afforded 180 calendar days to regain compliance with the bid price requirement. In order to regain compliance, the bid price of our common stock must close at a price of at least $ 1. 00 per share for a minimum of 10 consecutive trading days within the 180- day grace period. In the event the Company does not regain compliance by the end of the Compliance Period, the Company may be eligible for additional time to regain compliance (the Second Compliance Period) pursuant to Nasdaq Listing Rule 5810 (c) (3) (A) (i) by transferring to the Nasdaq Capital Market. To qualify for the Second Compliance Period, the Company would need to submit a transfer application and pay an application fee. In addition, the Company would be required to meet the continued listing requirement for the market value of its publicly held shares and all other initial listing standards for Nasdaq, with the exception of the bid price requirement, and will need to provide written notice of its intention to cure the deficiency during the Second Compliance Period, by effecting a reverse stock split, if necessary. There can be no assurance that the Company will be eligible for the Second Compliance Period, if applicable, or that the Staff would grant the Company' s request for continued listing subsequent to any delisting notification and there can be no assurance that the Company will be able to regain or maintain compliance with the minimum bid price requirement or any other Nasdaq listing standards, if applicable. If we fail to regain compliance, our common stock will be subject to delisting. Delisting from Nasdaq could adversely affect our ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities.** Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance. Our quarterly and annual operating results may fluctuate significantly in the future due to a variety

of ~~other~~ factors, many of which are outside of our control and may be difficult to predict. The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period- to- period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval. As of December 31, ~~2023~~ **2024** , our executive officers, directors, holders of 5 % or more of our capital stock and their respective affiliates beneficially owned approximately ~~57~~ **47** % of our common stock. These stockholders, acting together, may be able to control matters requiring stockholder approval. For example, they may be able to control elections of directors, amendments of our organizational documents or approval of any merger or other major corporate transactions. This concentration of ownership may delay, discourage or prevent a change of control, including unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as a stockholder, entrench our management and board of directors or delay or prevent a merger, takeover or other business combination involving us that other stockholders may desire. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders ~~,~~ and might affect the prevailing market price for our common stock. Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall. Sales of a substantial number of shares of our common stock in the public market could occur at any time. For example, we filed a shelf registration statement on Form S- 3 that became effective on August 17, 2022, which allows us to undertake various equity and debt offerings up to $ 300. 0 million (the Shelf Registration), and as of December 31, ~~2023~~ **2024** , we have sold ~~25~~ **34** , ~~965~~ **854** , ~~483~~ **373** shares of our common stock and pre- funded warrants to purchase ~~6~~ **8** , ~~236~~ **458** , ~~693~~ **964** shares of our common stock **pursuant to the Shelf Registration. In addition, on March 5, 2025, we completed an underwritten public offering of 75, 000, 000 units, with each unit consisting of one share of our common stock, a warrant to purchase one share of common stock, and a warrant to purchase one- half share of common stock,** pursuant to the Shelf Registration. Moreover, certain holders of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act, would result in the shares becoming freely tradeable in the public market, subject to the restrictions of Rule 144 in the case of our affiliates. If these shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. We will incur costs as a result of operating as a public company, and our management will devote substantial time to related compliance initiatives. Additionally, if we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired. As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes- Oxley Act, the Dodd- Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and the Nasdaq ~~Stock Market LLC (Nasdaq)~~ . As a result of our initiatives to comply with such regulatory requirements, we incur significant legal, accounting and other expenses which may increase after we are no longer an " emerging growth company. " Moreover, our management and other personnel need to devote a substantial amount of time to these compliance initiatives. In particular, as a public company we are required to comply with SEC rules that implement Section 404 of the Sarbanes- Oxley Act. Under these rules, we are required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm, unless we continue to qualify as a " smaller reporting company " at such time. To achieve compliance with Section 404 within the prescribed periods, we engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially continue to engage outside consultants and adopt a detailed work plan to assess and document the adequacy of our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively, and implement a continuous reporting and improvement process for internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadlines imposed by the Sarbanes- Oxley Act. Our internal control over financial reporting will not prevent or detect all errors and all fraud or prevent material weaknesses from being identified in such reporting. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system' s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. If we are not able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities. We may be subject to securities litigation, which is expensive and could divert management attention. The market price of our common stock **has been and** may **continue to** be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. This risk is especially relevant for us because biotechnology companies have experienced significant stock price

volatility in recent years and we may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management' s attention from other business concerns, which could seriously harm our business. Provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock. Our certificate of incorporation and bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. These provisions, among other things: • establish a classified board of directors so that not all members of our board are elected at one time; • permit only the board of directors to establish the number of directors and fill vacancies on the board; • provide that directors may only be removed " for cause "; • authorize the issuance of " blank check " preferred stock that our board could use to implement a stockholder rights plan (also known as a poison pill); • eliminate the ability of our stockholders to call special meetings of stockholders; • prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders; • prohibit cumulative voting; • authorize our board of directors to amend the bylaws; • establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and • require a super- majority vote of stockholders to amend or repeal specified provisions of our certificate of incorporation and bylaws. In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL), prohibits a publicly- held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15 % of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner or certain other conditions are met. Any provision of our certificate of incorporation, bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock. Our bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America are 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 bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for the following (except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court or for which such court does not have subject matter jurisdiction): • any derivative action or proceeding brought on our behalf; • any action asserting a claim of breach of fiduciary duty; • any action asserting a claim against us arising under the DGCL, our certificate of incorporation or our bylaws; 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 Exchange Act or any other claim for which the U. S. federal courts have exclusive jurisdiction. Our bylaws further 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. 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. In addition, these exclusive- forum provisions may impose additional litigation costs for stockholders who determine to pursue any such lawsuits against us. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find either exclusive- forum provision in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.