Risk Factors Comparison 2024-03-19 to 2023-03-28 Form: 10-K

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The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward- looking statements we have made in this Annual Report on Form 10- K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10- K and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations. Selected Risks Affecting Our Business Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are more fully described in this " Risk Factors " section, including the following: • We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability. ~~These factors raise substantial doubt regarding our ability to continue as a going concern.~~ • We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy. • We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability. • We are very early in our development efforts and all of our product candidates are in preclinical or clinical development. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidates for these or any other indications, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed. • Because gene therapy is novel and 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. • We intend to identify and develop novel gene therapy product candidates, which makes it difficult to predict the time, cost and potential success of product candidate development. • The regulatory approval processes of the U. S. Food and Drug Administration, or FDA, **the** European **Commission** ~~Medicines Agency, or the EMA,~~ and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed. • We have not yet completed testing of any product candidates in clinical trials. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials. • We may not be successful in our efforts to build a pipeline of additional product candidates or our next- generation platform technologies. • ~~Our~~ **Unfavorable conditions in our industry or the global economy could limit our ability to grow our** business and **negatively affect our results of** operations ~~could be adversely affected by the effects of health epidemics, including the COVID- 19 pandemic~~. • Gene therapies are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business. • We and our contract manufacturers for AAV9 are subject to significant regulation with respect to manufacturing our products. The third- party manufacturing facilities on which we rely, and any manufacturing facility that we may have in the future, may have limited capacity or fail to meet the applicable stringent regulatory requirements. • We currently rely exclusively on our collaboration with UT Southwestern for our preclinical research and development programs, including for discovering, preclinically developing and conducting all IND- enabling studies for our lead product candidates and our near- term future pipeline. Failure or delay of UT Southwestern to fulfill all or part of its obligations to us under the agreement, a breakdown in collaboration between the parties or a complete or partial loss of this relationship would materially harm our business. • UT Southwestern has entered into collaborations with third parties, including certain of our competitors, addressing targets and disease indications outside the scope of our collaboration. As a result, UT Southwestern may have competing interests with respect to their priorities and resources. • Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact the development or commercial success of our current and future product candidates. • We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively. • Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain. • **We may be subject to legal proceedings from time to time which seek material damages. •** Our term loan agreement contains restrictions that potentially limit our flexibility in operating our business, and we may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect. • If we are unable to obtain or protect intellectual property rights related to any of our product candidates, we may not be able to compete effectively in our market. Risks Related to our Financial Position and Capital Needs Since our inception, we have incurred significant net losses, and we expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses were $ **111. 6 million and $** 166. 0 ~~million and $ 174. 5~~ million for the years ended December 31, **2023 and** 2022 ~~and 2021~~, respectively. As of December 31, ~~2022~~ **2023**, we had an accumulated deficit of $ ~~401~~ **513**. ~~4~~ **0** million. We have financed our operations with $ ~~438~~ **589**. ~~5~~ **0** million in gross proceeds from equity financings, including from ~~our initial public offering, or the IPO, the sale of common stock pursuant to our Sales Agreement by and among Goldman Sachs & Co. LLC, SVB Securities LLC (f / k / a SVB Leerink LLC), Wells Fargo Securities, LLC and us, dated as of October 5, 2021, as amended by Amendment No. 1 to Sales Agreement, dated March 30, 2022, or the Sales Agreement, the sale of common stock pursuant to our Underwriting Agreement, or the Underwriting Agreement, with Goldman Sachs & Co. LLC, or the Underwriter, dated as of October 26, 2022, or the Follow- on Offering,~~ pre-

IPO private placements of convertible preferred stock, **our initial public offering, or the IPO, and subsequent sales of common stock in public and private securities offerings,** from our **previous** loan agreement with Silicon Valley Bank and **our current loan agreement with Trinity Capital and** from the option agreement dated October 21, 2022, or the Option Agreement, with Audentes Therapeutics, Inc. (d / b / a Astellas Gene Therapy), or Astellas, and the securities purchase agreement dated October 21, 2022, or the Securities Purchase Agreement (and together with the Option Agreement, the Astellas Transactions), with Astellas. We have no products approved for commercialization and have never generated any revenue from product sales. All of our product candidates are still in the clinical or preclinical development stage. We expect to continue to incur significant expenses and operating losses over the next several years. We expect that it could be several years, if ever, before we have a commercialized product. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we: • continue to advance the preclinical and clinical development of our product candidates and preclinical and discovery programs; • conduct our ongoing clinical trials of TSHA- 102 ~~, TSHA- 120~~ and any other current and future product candidates that we advance; • seek regulatory approval for any product candidates that successfully complete clinical trials; • continue to develop our gene therapy product candidate pipeline and next- generation platforms; • scale up our clinical and regulatory capabilities; • manufacture current good manufacturing practice, or cGMP, material for clinical trials or potential commercial sales; • establish a commercialization infrastructure and scale up internal and external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval; • adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products; • maintain, expand and protect our intellectual property portfolio; • hire additional clinical, manufacturing quality control, regulatory, manufacturing and scientific and administrative personnel; • add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and • incur additional legal, accounting and other expenses in operating as a public company. In ~~2022~~ **2023**, we generated revenue from the Astellas Transactions; however, to date we have not generated any revenue from product sales. To become and remain profitable, we must succeed in developing and eventually commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval, and manufacturing, marketing and selling any product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities and all of our product candidates are in clinical or preclinical development. We may never succeed in these activities and, even if we do, may never generate any revenue or revenue that is significant enough to achieve profitability. Even if we 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment ~~. These and other factors raise substantial doubt regarding our ability to continue as a going concern, which may create negative reactions to the price of our common stock. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our financial statements, and it is likely that investors will lose all or a part of their investment. Further, the perception that we may be unable to continue as a going concern may impede our ability to pursue strategic opportunities or operate our business due to concerns regarding our ability to discharge our contractual obligations. In addition, if there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms, or at all~~ . We are a clinical- stage gene therapy company with a limited operating history. We commenced operations in 2019, and our operations to date have been largely focused on organizing and staffing our company, business planning, raising capital and entering into collaboration and license agreements for conducting preclinical research and development activities for our product candidates and gene therapy pipeline. To date, we have not yet demonstrated our ability to successfully complete clinical trials, including pivotal clinical trials, obtain regulatory approvals, manufacture a product on a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to develop commercial capabilities, and we may not be successful in doing so. Our operations have consumed substantial amounts of cash since inception. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time- consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. We expect to continue to incur significant expenses and operating losses over the next several years as we conduct clinical trials of our product candidates, initiate future clinical trials of our product candidates, advance our preclinical programs, seek marketing approval for any product candidates that successfully complete clinical trials and advance any of our other product candidates we may develop or otherwise acquire. In addition, our product candidates, if approved, may not achieve commercial success. Our revenue, if any, primarily will be derived from sales of products that we do not expect to be commercially available for a number of years, if at all. If we obtain marketing approval for any product candidates that we develop or otherwise acquire, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We also expect an increase in our expenses associated with creating additional infrastructure to support operations as a public company. As of December 31, ~~2022~~ **2023**, we had cash and cash equivalents of $ ~~87~~ **143** . 9 million. We believe that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital requirements into ~~the first quarter of 2024~~ **2026** . This estimate is based on assumptions that may prove to be wrong, and we could use our

available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional product candidates, and changes in regulation. Our future capital requirements will depend on many factors, including: • the scope, progress, costs and results of discovery, preclinical development, laboratory testing and clinical trials for TSHA- 102 ~~; TSHA- 120~~ and any current and future product candidates that we advance; • our ability to access sufficient additional capital on a timely basis and on favorable terms, including with respect to our term loan facility with **Trinity Capital** ~~Silicon Valley Bank~~ ; • the extent to which we develop, in- license or acquire other product candidates and technologies in our gene therapy product candidate pipeline; • the costs and timing of process development and manufacturing scale- up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development; • the number and development requirements of product candidates that we may pursue; • the costs, timing and outcome of regulatory review of our product candidates; • our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure; • the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval; • the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property- related claims; • the **costs incurred in defending ourselves in any legal proceedings that we may be subject to; • the** revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and • the costs of operating as a public company. We will require additional capital to achieve our business objectives, including to conduct our ongoing and planned clinical trials of our product candidates. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long- term business strategy. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, including decades- high inflation and concerns of a recession in the United States or other major markets, and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide, including from the COVID- 19 pandemic. Weakness and volatility in the capital markets and the economy in general could also increase our costs of borrowing. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy. Our existing indebtedness contains restrictions that potentially limit our flexibility in operating our business. In addition, we may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect, or we may be unable to draw down the remaining tranches under our Term Loan Agreement if we are unable to satisfy certain conditions. On ~~August 12~~ **November 13** , ~~2021~~ **2023** , we entered into a Loan and Security Agreement, or the **Trinity** Term Loan Agreement, with the lenders party thereto from time to time, or the **Trinity** Lenders, and ~~Silicon Valley Bank~~ **Trinity Capital Inc.** , as administrative agent and collateral agent for the **Trinity** Lenders, or **Trinity** ~~the Agent~~ , which provides for term loans of up to $ ~~100~~ **40** . 0 million in the aggregate available in ~~four~~ **a single** ~~tranches~~ **tranche** . The **Trinity** Term Loan Agreement contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things: • incur or assume certain debt; • merge or consolidate or acquire all or substantially all of the capital stock or property of another entity; • change the nature of our business; • change our organizational structure or type; • license, transfer, or dispose of certain assets; • grant certain types of liens on our assets; • make certain investments; • pay cash dividends; and • enter into material transactions with affiliates. A breach of any of these covenants could result in an event of default under the **Trinity** Term Loan Agreement. An event of default will also occur if, among other things, a material adverse change in our business, operations, or condition occurs, which could potentially include a material impairment of the prospect of our repayment of any portion of the amounts we owe under the Term Loan Agreement. In the case of a continuing event of default under the **Trinity** Term Loan Agreement, the **Trinity** ~~lenders~~ **Lenders** could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted the **Trinity** Lenders a security interest under the Term Loan Agreement, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the **Trinity** Term Loan Agreement are secured by all of our existing and future assets, ~~excluding~~ **including** intellectual property ~~, which is subject to a negative pledge arrangement~~ . At closing, we drew ~~on~~ **the full** $ ~~30~~ **40** . 0 million ~~of the $ 40. 0 million available to us as part of the first tranche. We drew the remaining $ 10. 0 million available under the first tranche on December 29, 2021~~ . We may not have enough available cash to repay or refinance our indebtedness at the time any such repayment is required. In such an event, we may be required to delay, limit, reduce, or terminate our preclinical and clinical product development or commercialization efforts or grant others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition, and results of operations could be materially adversely affected as a result. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, government or private party grants, debt financings and license and collaboration agreements. We do not currently have any other committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or product candidates, grant licenses on terms that may not be favorable to us or commit to future payment streams. If we are unable to raise additional funds through equity or debt financings when needed, 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.

Adverse developments affecting financial institutions, companies in the financial services industry or the financial services industry generally, such as actual events or concerns involving liquidity, defaults or non- performance, could adversely affect our operations and liquidity. Actual events involving limited liquidity, defaults, non- performance or other adverse developments that affect financial institutions or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank, or SVB, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or the FDIC, as receiver. Although a statement by the U. S. Department of the Treasury, the Federal Reserve and the FDIC stated that all depositors of SVB would have access to all of their money after only one business day following the date of closure, uncertainty and liquidity concerns in the broader financial services industry remain. Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. The U. S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $ 25 billion of loans to financial institutions secured by such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments. However, widespread demands for customer withdrawals or other needs of financial institutions for immediate liquidity may exceed the capacity of such program. There is no guarantee that the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions in a timely fashion or at all. Our access to our cash and cash equivalents in amounts adequate to finance our operations could be significantly impaired by the financial institutions with which we have arrangements directly facing liquidity constraints or failures. In addition, investor concerns regarding the U. S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any material decline in available funding or our ability to access our cash and cash equivalents could adversely impact our ability to meet our operating expenses, result in breaches of our contractual obligations or result in violations of federal or state wage and hour laws, any of which could have material adverse impacts on our operations and liquidity. Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy ~~and~~ **. Unfavorable conditions** in the **economy both** ~~global financial markets, including decades- high inflation and concerns of a recession~~ in the United States ~~or~~ **and abroad, including conditions resulting from changes in gross domestic product growth in** ~~other -- the major~~ **United States or abroad, financial and credit** ~~markets -~~ **market fluctuations** ~~. For example -~~, **inflation, rising interest rates, international trade relations, political turmoil, natural catastrophes, outbreaks of contagious diseases, such as** the COVID- 19 pandemic **, warfare and terrorist attacks on the United States, Europe, the Asia Pacific region or elsewhere, such** ~~has -~~ **as the conflict in the Middle East, could** ~~caused -~~ **cause** ~~extreme volatility and~~ **a decrease in business investments,** ~~disruptions ---~~ **disrupt** ~~in~~ the ~~capital~~ **timing** and ~~credit~~ **cadence of key industry events, and negatively affect the growth of our business and our results of operations. For example, the COVID- 19 pandemic adversely affected workforces, economies and financial** markets **globally** ~~. In addition -~~, **leading to a reduction in the ability of, or the inability of, partners, suppliers, vendors or other parties to meet their contractual obligations, and for a period of time, a reduction in customer spending on technology, and such conditions may reoccur in the future. The war in Ukraine and the related political and economic responses imposed on** Russia **such as sanctions** ~~' s invasion of Ukraine may lead to a prolonged~~ , **may also exacerbate these issues** ~~adverse impact on global economic, social~~ and ~~market conditions~~ **trends especially in Europe** . A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third- party payors or our collaborators. ~~For example, while we do not have any current operations in Ukraine or Russia, we do not know the extent to which Russia' s invasion of Ukraine could impact any of our current suppliers and their ability to provide us with supplies and services.~~ Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business, financial condition, results of operations and prospects. Risks Related to the Development of our Product Candidates **TSHA- 102 is currently our lead product candidate and there is no guarantee that we will be able to successfully develop and commercialize TSHA- 102. We are currently focused on the potential development of our lead product candidate, TSHA- 102. We are still developing TSHA- 102 and it cannot be marketed or sold in the United States or in foreign markets until regulatory approval has been obtained from the FDA or applicable foreign regulatory agencies. The process of obtaining regulatory approval is expensive and time consuming. The FDA and foreign regulatory authorities may never approve TSHA- 102 for sale and marketing, and even if TSHA- 102 is ultimately approved, regulatory approval may be delayed or limited in the United States or in other jurisdictions. Even if we are authorized to sell and market TSHA- 102 in one or more markets, there is no assurance that we will be able to successfully market TSHA- 102 or that TSHA- 102 will achieve market acceptance sufficient to generate profits. If we are unable to successfully develop and commercialize TSHA- 102 due to failure to obtain regulatory approval for TSHA-102, to successfully market TSHA- 102, to generate profits from the sale of TSHA- 102, or due to other risk factors outlined in this report, it would have material adverse effects on our business, financial condition, and results of operations as TSHA- 102 is currently our sole product candidate.** We are very early in our development efforts and all of our product candidates are in clinical or preclinical development. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidates for these or any other indications, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed. We are very early in our

development efforts and all of our product candidates are still in clinical or preclinical development. Each of our programs and product candidates will require additional preclinical and / or clinical development, regulatory approval, obtaining manufacturing supply, capacity and expertise, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts before we generate any revenue from product sales. We do not have any products that are approved for commercial sale, and we may never be able to develop or commercialize marketable products. Our ability to generate revenue from our product candidates, which we do not expect will occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our product candidates. The success of TSHA- 102 ~~, TSHA- 120~~ or any other product candidates that we develop or otherwise may acquire will depend on several factors, including: • effective ~~investigational new drug applications, or~~ INDs ~~,~~ from the FDA or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for our product candidates; • successful enrollment and completion of clinical trials, including under the FDA' s **and comparable foreign regulatory authorities'** current good clinical practices, or GCPs, and current Good Laboratory Practices; • timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable, and clinical trials; • sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials; • successful development of, or making arrangements with third- party manufacturers for, our commercial manufacturing processes for any of our product candidates that receive regulatory approval; • receipt of timely marketing approvals from applicable regulatory authorities; • launching commercial sales of products, if approved, whether alone or in collaboration with others; • acceptance of the benefits and use of our products, including method of administration, if approved, by patients, the medical community and third- party payors, for their approved indications; • the prevalence and severity of adverse events experienced with TSHA- 102 ~~and TSHA- 120~~ or any other product candidates; • the availability, perceived advantages, cost, safety and efficacy of alternative therapies for any product candidate, and any indications for such product candidate, that we develop; • our ability to produce TSHA- 102 ~~and TSHA- 120~~ or any other product candidates we develop on a commercial scale; • obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio; • maintaining compliance with regulatory requirements, including cGMPs, and complying effectively with other procedures; • obtaining and maintaining third- party coverage and adequate reimbursement and patients' willingness to pay out- of- pocket in the absence of such coverage and adequate reimbursement; and • maintaining a continued acceptable safety, tolerability and efficacy profile of the products following approval. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize the product candidates we develop, which would materially harm our business. If we do not receive marketing approvals for any product candidate we develop, we may not be able to continue our operations. Our strategy is to identify, develop and commercialize gene therapy product candidates using an AAV9 capsid for intrathecal delivery of therapeutic transgenes to certain kinds of cells. Our future success depends on the successful development of these novel therapeutic approaches. To date, very few products that utilize gene transfer have been approved in the United States **, the EU** or **other** ~~Europe~~ **European countries** and no gene therapy products that utilize an intrathecal method of administration have been approved. There have been a limited number of clinical trials of gene transduction technologies, with only two product candidates ever approved by the FDA. Although AAV9 has been tested in numerous clinical trials and is used in two currently approved products, we cannot be certain that our AAV9 product candidates will successfully complete preclinical studies and clinical trials, or that they will not cause significant adverse events or toxicities. We also cannot be certain that we will be able to avoid triggering toxicities in our future preclinical studies or clinical trials or that our intrathecal method of administration will not cause unforeseen side effects or other challenges. Any such results could impact our ability to develop a product candidate, including our ability to enroll patients in our clinical trials. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our approach to gene therapy, or any similar or competitive programs, will result in the identification, development, and regulatory approval of any product candidates, or that other gene therapy programs will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to our current gene therapy product candidates or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays and challenges in achieving sustainable, reproducible, and scalable production. Any of these factors may prevent us from completing our preclinical studies or clinical trials or commercializing any product candidates we may develop on a timely or profitable basis, if at all. The regulatory requirements that will govern any novel gene therapy product candidates we develop are not entirely clear and are subject to change. Within the broader genetic medicine field, very few therapeutic products have received marketing authorization from the FDA or the ~~EMA~~ **European Commission** . Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or 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 institutional review boards, or IRBs, under guidelines promulgated by the National Institutes of Health, or NIH, gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or 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 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~~ **Similar considerations apply** in the European Union. The EMA' s Committee for Advanced Therapies, or 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 European Union, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU **legislation and** 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 may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point. 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, the ~~EMA~~ **EU** , and other regulatory ~~bodies~~ **authorities** to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the ~~EMA~~ **EU** , **national competent authorities of EU Member States** 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, the EMA or **the European Commission or** other regulatory ~~bodies~~ **authorities** 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 **the European Commission or** other regulatory authorities. Regulatory ~~agencies~~ **authorities** 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~~ **authority** may not be indicative of what other regulatory ~~agencies~~ **authorities** 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 these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future 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 any product candidates we identify and develop. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all. Preclinical studies and clinical trials are expensive, time- consuming, difficult to design and implement and involve an uncertain outcome. Further, we may encounter substantial delays in completing the development of our product candidates. All of our product candidates are in clinical or preclinical development and their risk of failure is high. The clinical trials and manufacturing of our product candidates are, and the manufacturing and marketing of our products, if approved, will be, subject to extensive and rigorous review and regulation by numerous government **and regulatory** authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. In particular, because our product candidates are subject to regulation as biological products, we will need to demonstrate that they are safe, pure and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. Clinical testing is expensive and can take many years to complete and is subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Failure can occur at any time during the clinical trial process. Even if our future clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our product candidates for their targeted indications or support continued clinical development of such product candidates. Our future clinical trial results may not be successful. In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. This is particularly true for clinical trials in very rare diseases, such as with TSHA- 102 for the treatment of Rett syndrome ~~and TSHA- 120 for the treatment of GAN~~ , 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~~ required to exercise flexibility in approving therapies for such

diseases. For example, in January 2023, we reported feedback from the Type B end- of- Phase 2 meeting with the FDA following receipt of the formal meeting minutes. The FDA provided additional clarity for TSHA- 120 where MFM32 was acknowledged as an acceptable endpoint with a recommendation to dose additional patients in a double- blind, placebo- controlled design to support a BLA. The FDA acknowledged that our overall approach to manufacturing of commercial material was appropriate pending their review of our CMC module 3 amendment ~~recently~~ submitted for TSHA- 120. 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 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. To date, we have not completed any clinical trials required for the approval of our product candidates. We may experience delays in conducting any clinical trials and we do not know whether our clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Events that may prevent successful or timely completion of clinical development include: • 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 advanced clinical trials, including our natural history studies; • delays in developing suitable assays for screening patients for eligibility for trials with respect to certain product candidates; • delays in reaching agreement with the FDA, EMA or other regulatory authorities as to the design or implementation of our clinical trials; • obtaining regulatory approval to commence a clinical trial; • reaching an agreement on acceptable terms with clinical trial sites or prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical trial sites; • obtaining IRB approval **and positive Ethics Committee opinions** at each trial site; • recruiting suitable patients to participate in a clinical trial; • having patients complete a clinical trial or return for post- treatment follow- up; • clinical sites, CROs or other third parties deviating from trial protocol or dropping out of a trial; • failure to perform in accordance with the FDA' s GCP requirements, or applicable regulatory guidelines in other countries; • addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits; • adding a sufficient number of clinical trial sites; or • manufacturing sufficient quantities of product candidate for use in clinical trials. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including: • we may experience changes in regulatory requirements or guidance, or receive feedback from regulatory authorities that requires us to modify the design of our clinical trials; • clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs; • the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate; • our third- party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; • we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non- compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks; • the cost of clinical trials of our product candidates may be greater than we anticipate and we may not have funds to cover the costs; • the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; • regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and • any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may: • incur unplanned costs; • be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all; • obtain marketing approval in some countries and not in others; • obtain marketing approval for indications or patient populations that are not as broad as intended or desired; • obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings or Risk Evaluation and Mitigation Strategies, or REMS **, or comparable foreign strategies** ; • be subject to additional post- marketing testing requirements; or • have the product removed from the market after obtaining marketing approval. We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs **or Ethics Committees** of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA, ~~EMA~~ **the competent authorities of EU Member States** or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, ~~EMA~~ **the competent authorities of EU Member States** or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. All of our product candidates will require extensive clinical testing before we are prepared to submit a BLA or marketing authorization application, or MAA, for regulatory approval. We cannot predict with any certainty if or when we might complete the clinical development for our product candidates and submit a BLA or MAA for regulatory approval of any of our product candidates or whether any such BLA or MAA will be approved. We may also seek feedback from the FDA, EMA or other regulatory authorities on our clinical development program, and the FDA, EMA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could

further delay our development programs. We cannot predict with any certainty whether or when we might complete a given clinical trial. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be harmed, and our ability to generate revenues from our product candidates may be delayed or lost. In addition, any delays in our clinical trials could increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. The regulatory approval processes of the FDA, ~~EMA~~ **European Commission** and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed. The time required to obtain approval or other marketing authorizations by the FDA, ~~EMA~~ **European Commission** and comparable foreign authorities is unpredictable, and it typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, and 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. We have not obtained regulatory approval for any product candidate, and it is possible that we may never obtain regulatory approval for any product candidates we may seek to develop in the future. Neither we nor any current or future collaborator is permitted to market any drug product candidates in the United States until we receive regulatory approval of a BLA from the FDA, and we cannot market it in the European Union until we receive approval for a MAA from the ~~EMA~~ **European Commission** , or other required regulatory approval in other countries. To date, we have had only limited discussions with the FDA regarding clinical development programs or regulatory approval for any product candidate within the United States. In addition, we have only had limited discussions with Health Canada, and no discussions with the EMA and other comparable foreign authorities, regarding clinical development programs or regulatory approval for any product candidate outside of the United States. Prior to obtaining approval to commercialize any drug product candidate in the United States or abroad, we must demonstrate with substantial evidence from well- controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory ~~agencies~~ **authorities** , that such product candidates are safe, pure and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA **or comparable foreign regulatory authorities** may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs. Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval and marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval and marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects. We have invested a significant portion of our time and financial resources in the development of our preclinical product candidates. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize TSHA- 102 ~~, TSHA- 120~~ and any future product candidates in a timely manner. Even if we eventually complete clinical testing and receive approval of a BLA or foreign marketing application for TSHA- 102 ~~, TSHA- 120~~ or any future product candidates, the FDA, ~~EMA~~ **European Commission** or the applicable foreign regulatory ~~agency~~ **authority** may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post- marketing clinical trials. The FDA, ~~EMA~~ **European Commission** or the applicable foreign regulatory ~~agency~~ **authority** also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA, ~~EMA~~ **European Commission** or applicable foreign regulatory ~~agency~~ **authority** may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects. In addition, the FDA, ~~EMA~~ **EU and related regulatory authorities** and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. We have not yet completed testing of any product candidate in clinical trials. Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical or animal studies and early clinical trials does not ensure that later large- scale efficacy trials will be successful nor does it predict final results. For example, we may be unable to identify suitable animal disease models for our product candidates, which could delay or frustrate our ability to proceed into clinical trials or obtain marketing approval. 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. **Our** ~~Further, our~~ Phase 1 / 2 clinical trials of TSHA- 102 ~~and TSHA- 120~~ will involve small patient populations. Because of the small sample sizes, the results of these trials may not be indicative of results of future clinical trials. Further, although other gene therapy clinical trials conducted by others also utilized AAV9 vectors, these trials should not be relied upon as evidence that our

planned clinical trials will succeed. 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. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects. Interim " top- line " and preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publish interim top- line or preliminary results from our clinical trials. Interim results 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. Preliminary or top- line results 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, interim and preliminary data should be viewed with caution until the final data are available. **For example, we have announced initial clinical observations from the first patients treated in the Phase 1 / 2 REVEAL trial of TSHA- 102. However, those observations may not endure or be repeated in subsequently dosed patients or any age or disease severity, including patients receiving higher doses of TSHA- 102. Initial clinical observations also may not translate into success on primary endpoints of the REVEAL trial through week 52.** Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly **. Further, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the approvability or commercialization of the particular product candidate or product and our business 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 the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, product candidate or our business. If the top- line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize any of our product candidates, our business, operating results, prospects or financial condition may be harmed** . Our preclinical studies and clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious adverse or unacceptable side effects may be identified during the development of our product candidates, which could prevent or delay regulatory approval and commercialization, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates. Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe, pure and effective for use in each target indication, and failures can occur at any stage of testing. Preclinical studies and clinical trials often fail to demonstrate safety or efficacy of the product candidate studied for the target indication. Further, the patients evaluated in our clinical trials are often seriously ill. For example, a patient in our clinical trial of TSHA- 101 succumbed to pneumonia and pleural effusion with a concomitant hospital- acquired MRSA infection, which was deemed by the principal investigator and independent DSMB not to be drug related. Any side effects or patient deaths could affect the development of our product candidates, even if deemed to not be drug related. Among the risks in any gene therapy product based on viral vectors are the risks of immunogenicity, elevated liver enzymes and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation. While new AAV vectors have been developed to reduce side effects previously reported in third- party gene therapy treatments, and AAV9 has been generally well tolerated in clinical trials and in approved products, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration, which, while not necessarily adverse to the patient' s health, could substantially limit the effectiveness of the treatment. For example, in previous third- party clinical trials involving other AAV vectors for gene therapy, some subjects experienced the development of a T- cell antibody response, whereby after the vector is within the target cells, the cellular immune response system triggers the removal of transduced cells by activated T- cells. Other preclinical studies have suggested that high dosages of AAV administration may result in toxicity due to degeneration of the DRG. If our vectors demonstrate a similar effect in other programs, we may decide or be required to perform additional preclinical studies or to halt or delay further clinical development of our product candidates. In addition to side effects caused by the product candidate, the administration process or related procedures also can cause adverse side effects. Each of our lead product candidates are expected to be administered by intrathecal injection. While this method of administration has been available for decades, its use for therapies is relatively new, no gene therapy is currently approved for intrathecal administration, and it may be perceived as having greater risk than more common methods of administration, such as intravenous injection. If any such adverse events occur, our clinical trials could be suspended or terminated. If we cannot demonstrate that any adverse events were not caused by the drug or administration process or related procedures, the FDA ~~, EMA~~ or foreign regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product- related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate,

delay, suspend or terminate any future clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly. If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective. The FDA **, comparable foreign regulatory authorities,** or an IRB **or Ethics Committee** may also require that we suspend, discontinue, or limit our clinical trials based on safety information, or that we conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates or limiting the scope of the approved indication, if approved. Many product candidates that initially showed promise in early- stage testing have later been found to cause side effects that prevented further development of the product candidate. Additionally, if one or more of our product candidates receives marketing approval, and we or others identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including: • regulatory authorities may withdraw **, vary or suspend** approvals of such product; • regulatory authorities may require additional warnings on the labels; • we may be required to create a medication guide outlining the risks of such side effects for distribution to patients or other requirements subject to a REMS **or comparable foreign strategies** ; • we could be sued and held liable for harm caused to patients; • we may not be able to achieve or maintain third- party payor coverage and adequate reimbursement; and • our reputation and physician or patient acceptance of our products may suffer. There can be no assurance that we will resolve any issues related to any product- related adverse events to the satisfaction of the FDA or foreign regulatory ~~agency~~ **authority** in a timely manner or at all. Moreover, any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects. As an organization, we have never conducted pivotal clinical trials, and may be unable to do so for any product candidates we may develop, including TSHA- 102 ~~and TSHA- 120~~ . We will need to successfully complete our ongoing and planned clinical trials, including pivotal clinical trials, in order to obtain FDA **and comparable foreign regulatory** approval to market our product candidates. Carrying out later- stage clinical trials and the submission of a successful BLA **and comparable foreign application** is a complicated process. As an organization, we have initiated ~~three~~ Phase 1 / 2 clinical trials, have not previously conducted any later stage or pivotal clinical trials, **but** have limited experience in preparing, submitting and prosecuting regulatory filings and have not previously submitted a BLA **or comparable foreign application** for any product candidate. In addition, we have had limited interactions with the FDA **comparable foreign regulatory authorities** and cannot be certain how many additional clinical trials of our product candidates will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA submission **or comparable foreign application** and approval of any product candidate. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates. The disorders we seek to treat have low prevalence and it may be difficult to identify and enroll patients with these disorders. If we experience delays or difficulties in the enrollment and / or maintenance of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population and competition for patients with other trials. Genetic diseases generally, and especially the rare diseases for which some of our current product candidates are targeted, have low incidence and prevalence. For example, the estimated addressable patient population with typical Rett syndrome caused by a pathogenic / likely pathogenic MECP2 mutation is between 15, 000 and 20, 000 patients in the United States, European Union and United Kingdom, and accordingly it may be difficult for us to identify and timely recruit a sufficient number of eligible patients to conduct our clinical trials. Further, any natural history studies that we or our collaborators may conduct may fail to provide us with patients for our clinical trials because patients enrolled in the natural history studies may not be good candidates for our clinical trials, or may choose to not enroll in our clinical trials. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. 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 as required by the FDA, EMA or foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including: • the eligibility criteria for the trial in question; • the size of the patient population and process for identifying patients; • the perceived risks and benefits of the product candidate in the trial, including relating to AAV9- based gene therapy approaches and intrathecal delivery systems; • the availability of competing commercially available therapies and other competing therapeutic candidates' clinical trials; • the willingness of patients to be enrolled in our clinical trials; • the efforts to facilitate timely enrollment in clinical trials; • potential disruptions caused by ~~the COVID- 19~~ **public health crises, such as** ~~pandemic~~ **pandemics or similar outbreaks** , including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors; • the patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; and • the proximity and availability of clinical trial sites for prospective patients. Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely

conduct of our clinical trials and we will have limited influence over their performance. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials. We may seek orphan drug designation for some of our product candidates and we may be unsuccessful, or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity, for product candidates for which we obtain orphan drug designation. Regulatory authorities in some jurisdictions, including the United States, may designate drugs or biologics intended to treat relatively small patient populations as orphan drug products. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals in the United States, or a patient population of 200, 000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitled a party to financial incentives such as tax advantages and user fee waivers. Opportunities for grant funding toward clinical trial costs may also be available for clinical trials of drugs or biologics for rare diseases, regardless of whether the drugs or biologics are designated for the orphan use. In addition, if a drug or biologic with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a seven year period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the " same drug " and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time. **In the EU, a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of life- threatening or chronically debilitating conditions; (ii) either (a) such conditions affect not more than 5 in 10, 000 persons in the EU when the application is made, or (b) the product without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition. Orphan medicinal product designation entitles an applicant to incentives such fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan medicinal products are entitled to a ten- year period of market exclusivity for the approved therapeutic indication, which means that the EMA cannot accept another marketing authorization application or accept an application to extend for a similar product and the European Commission cannot grant a marketing authorization for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product destination, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar medicinal product with the same orphan indication during the 10 year period if: (i) if the applicant consents to a second original orphan medicinal product application, (ii) if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities; or (iii) if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A company may voluntarily remove a product from the register of orphan products. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.** We have obtained orphan drug designation from the FDA for TSHA- 120 for the treatment of GAN, TSHA- 102 for the treatment of Rett syndrome ~~, TSHA- 101 for treatment of GM2 gangliosidosis~~ , and TSHA- 105 for the treatment of SLC13A5 deficiency. In addition, TSHA- 118 has received orphan drug designation for the treatment of CLN1 disease from the FDA and EMA. We may seek orphan designation for certain of our other current and future product candidates. However, we may be unsuccessful in obtaining orphan drug designation for these or other product candidates and may be unable to maintain the benefits associated with orphan drug designation. Even if we obtain orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect those product candidates from competition because different drugs can be approved for the same condition, and orphan drug exclusivity does not prevent the FDA **or comparable foreign regulatory authorities** from approving the same or a different drug in another indication. Even after an orphan drug is granted orphan exclusivity and approved, the FDA can subsequently approve a later application for the same drug for the same condition before the expiration of the seven- year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan- drug- exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. We have **obtained orphan drug designation from the FDA for TSHA- 120 for the treatment of GAN and TSHA- 102 for the treatment of Rett syndrome. We may seek orphan designation for certain of our other current and future product candidates. However, we may be unsuccessful in obtaining orphan drug designation for these or other product candidates and may be unable to maintain the benefits associated with orphan drug designation. Even if we obtain orphan drug exclusivity for any of our product candidates,**

that exclusivity may not effectively protect those product candidates from competition because different drugs can be approved for the same condition, and orphan drug exclusivity does not prevent the FDA or comparable foreign regulatory authorities from approving the same or a different drug in another indication. Even after an orphan drug is granted orphan exclusivity and approved, the FDA can subsequently approve a later application for the same drug for the same condition before the expiration of the seven- year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan- drug- exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. We have received rare pediatric disease designation for TSHA- 102 for the treatment of Rett syndrome ~~, TSHA- 105 for the treatment of SLC13A5 deficiency, TSHA- 118 for the treatment of CLN1 disease and TSHA- 120 for the treatment of GAN~~. However, a marketing application for TSHA- 102, ~~TSHA- 105 and TSHA- 118~~ if approved, may not meet the eligibility criteria for a PRV or the rare pediatric disease designation program may sunset before FDA is able consider us for a voucher. We have received rare pediatric disease designation for TSHA- ~~120 for the treatment of GAN, TSHA- 118 for the treatment of CLN1 disease, TSHA-~~ 102 for the treatment of Rett syndrome ~~and TSHA- 105 for the treatment of SLC13A5 deficiency~~. Designation of a drug or biologic as a product for a rare pediatric disease does not guarantee that a BLA for such drug or biologic will meet the eligibility criteria for a rare pediatric disease PRV at the time the application is approved. Under the FDCA, we will need to request a rare pediatric disease PRV in our original BLA for TSHA- 102, ~~TSHA- 105, TSHA- 118, TSHA- 120,~~ and any other candidates for which we submit a marketing application. The FDA may determine that ~~a~~ **such** BLA ~~for TSHA- 102, TSHA- 105, TSHA- 118, TSHA- 120~~, if approved, does not meet the eligibility criteria for a PRV, including for the following reasons: • ~~CLN1 disease,~~ Rett syndrome ~~, or SLC13A5 deficiency~~ no longer ~~meet~~ **meets** the definition of a rare pediatric disease; • the BLA contains an active ingredient that has been previously approved in a BLA; • the BLA is not deemed eligible for priority review; • the BLA does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population (that is, if the BLA does not contain sufficient clinical data to allow for adequate labeling for use by the full range of affected pediatric patients); or • the BLA is approved for a different adult indication than the rare pediatric disease for which TSHA- ~~120, TSHA- 118, TSHA-~~ 102 **is** ~~or TSHA- 105 are~~ designated. The authority for the FDA to award rare pediatric disease PRVs for drugs that have received rare pediatric disease designation prior to September 30, 2024 currently expires on September 30, 2026. ~~If~~ **Absent any extension through federal legislation, if** the BLA for TSHA- 102 ~~, TSHA- 105, TSHA- 118, TSHA- 120~~ is not approved prior to September 30, 2026 for any reason, regardless of whether it meets the criteria for a rare pediatric disease PRV, it will not be eligible for a PRV ~~. However, it is also possible the authority for FDA to award rare pediatric disease PRVs will be further extended through federal lawmaking. We have received fast track designation for TSHA- 118 for the treatment of CLN1 disease, and we may seek fast track designation for our other product candidates. Even if received, fast track designation may not actually lead to a faster review or approval process and does not increase the likelihood that our product candidates will receive marketing approval. We have received fast track designation for TSHA- 118 for the treatment of neurocognitive manifestations of the patients with CLN1 disease, and we may seek fast track designation for our other product candidates. If a drug or biologic is intended for the treatment of a serious or life- threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for FDA fast track designation for a particular indication. There is no assurance that the FDA will grant this status to any of our other proposed product candidates. If granted, fast track designation makes a product eligible for more frequent interactions with FDA to discuss the development plan and clinical trial design, as well as rolling review of the application, which means that the company can submit completed sections of its marketing application for review prior to completion of the entire submission. Marketing applications of products candidates with fast track designation may qualify for priority review under the policies and procedures offered by the FDA, but the fast track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast track designation does not provide any assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track designation at any time if it believes that the designation is no longer supported by data from our clinical development program~~. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and management resources, we must focus on development programs and product candidates that we identify for specific indications. As such, we are currently primarily focused on the development of TSHA- 102 (Rett syndrome) ~~and TSHA- 120 (GAN), each of which we have advanced into clinical development~~. As a result, we may forego or delay pursuit of opportunities with other product candidates, including TSHA- 101 (GM2 gangliosidosis), TSHA- 103 (SLC6A1), TSHA- ~~104 (SURF1), TSHA-~~ 105 (SLC13A5 deficiency), TSHA- 118 (CLN1 disease), and TSHA- 121 (CLN7) or for other indications for these product candidates that later prove to have greater commercial potential. Our resource allocation decisions, for example, our strategic prioritization in March 2022, may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable

rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. We are currently conducting our Phase 1 / 2 **adolescent and adult** trial of TSHA- 102 in Canada and plan to conduct in the future ~~conduct~~ additional clinical trials for our product candidates outside the United States, and the FDA and similar foreign regulatory authorities may not accept data from such trials. We are conducting our Phase **adolescent and adult** 1 / 2 clinical trial of TSHA- 102 in Canada and may in the future choose to conduct additional clinical trials outside the United States, including in the United Kingdom, ~~Europe~~ **European Union** or other foreign jurisdictions. The acceptance of trial data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on- site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. Additionally, the FDA' s clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any similar foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any similar foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time- consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction. We may not be successful in our efforts to build a pipeline of additional product candidates. Our business model is centered on developing therapies for patients with rare, monogenic central nervous system, or CNS, disorders by establishing focused selection criteria to select, develop and advance product candidates that we believe will have a high probability of technical and regulatory success through development into commercialization. We may not be able to continue to identify and develop new product candidates, including from our next- generation platform technologies, in addition to the pipeline of product candidates that we have established through our collaboration with UT Southwestern. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price. If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed. From time to time, we may estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of preclinical studies and clinical trials and the submission of regulatory filings, including IND / CTA submissions. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. ~~Our business and operations could be adversely affected by the effects of health epidemics, including the ongoing COVID- 19 virus, which was declared by the World Health Organization as a global pandemic. Remote work policies, quarantines, shelter- in- place and similar government orders, shutdowns or other restrictions on the conduct of business operations related to the COVID- 19 pandemic or other health epidemics may negatively impact productivity and may disrupt our ongoing research and development activities and our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. Further, such orders also may impact the availability or cost of materials, which would disrupt our supply chain and manufacturing efforts and could affect our ability to conduct ongoing and planned clinical trials and preparatory activities. We expect many employees to continue to work remotely or a hybrid of in- person and remote work, which presents risks, uncertainties and costs that could affect our performance, including operational and workplace culture challenges, uncertainty regarding office space needs and heightened vulnerability to cyberattacks. Although the timing and conduct of our current and planned clinical trials have not been impacted by the COVID- 19 pandemic to date, health epidemics, including the COVID- 19 pandemic, may affect the conduct of our clinical trials in the future, including: • delays, difficulties or a suspension in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • interruptions in our ability to manufacture and deliver drug supply for trials; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; • changes in local regulations as part of a response to the COVID- 19 outbreak that may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether; • interruption of key clinical trial activities, such as clinical trial site monitoring, and the ability or willingness of subjects to travel to trial sites due to limitations on travel imposed or recommended by federal or state governments, employers and others; • limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; • delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and • refusal of the FDA~~

~~to accept data from clinical trials in these affected geographies. We previously reported that a patient in our Phase 1 / 2 trial of TSHA- 101 may have contracted COVID- 19 after leaving the trial site. Although the principal investigator and independent DSMB deemed the patient' s death to not be drug related, in an abundance of caution for our patients we have made minor modifications to our trial protocol. Our financial results for the year ended December 31, 2021 were not impacted by COVID- 19. However, the spread of COVID- 19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID- 19 may be difficult to assess or predict, it has and could continue to result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID- 19 as well as related supply chain issues, labor shortages and rising inflation could materially affect our business and the value of our common stock. The global COVID- 19 pandemic continues to evolve. The extent to which the COVID- 19 pandemic impacts our business and operations, including our clinical development and regulatory efforts, will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as the continued geographic spread of the disease, the duration and effect of any future business disruptions in the United States and other countries to contain and treat patients with the disease and the availability, timing and effectiveness of a vaccine, both domestically and globally. Accordingly, we do not yet know the full extent of potential delays or impacts on our business, our clinical and regulatory activities, our manufacturing activities, healthcare systems or the global economy as a whole. However, these impacts could adversely affect our business, financial condition, results of operations and growth prospects. In addition, to the extent the ongoing COVID- 19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this " Risk Factors " section.~~ The United Kingdom' s withdrawal from the European Union may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union and require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union. **The** ~~Following the result of a referendum in 2016, the~~ United Kingdom ~~left~~ **' s, withdrawal from** the **EU** ~~European Union~~ on January 31, 2020, commonly referred to as Brexit ~~. Pursuant to~~ **, has changed** the **regulatory relationship** ~~formal withdrawal arrangements agreed~~ between the United Kingdom and the ~~European Union~~ **EU. The Medicines and Healthcare products Regulatory Agency** , **or MHRA, is now** the United Kingdom ~~was subject to a transition period until December 31~~ **' s standalone regulator for medicinal products and medical devices. Great Britain (England** , ~~2020~~ **Scotland and Wales) is now a third country to the EU. Northern Ireland will** , ~~during which European Union~~ **with regard to EU regulations, continue to follow the EU regulatory** rules ~~continued to apply. A trade and cooperation agreement, or for now. The the Trade and Cooperation Agreement, that outlines the future trading relationship between the~~ United Kingdom ~~and~~ **regulatory framework in relation to clinical trials is governed by** the ~~European Union applied provisionally~~ **Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which is derived** from **the CTD, as implemented into the United Kingdom national law through secondary legislation. On January 17, 2022, the MHRA launched an eight- week consultation on reframing the United Kingdom legislation for clinical trials, and which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The United Kingdom Government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will determine how closely the United Kingdom regulations will align with the CTR. In October 2023, the MHRA announced a new Notification Scheme for clinical trials which enables a more streamlined and risk- proportionate approach to initial clinical trial applications for Phase 4 and low- risk Phase 3 clinical trial applications. Marketing authorizations in the United Kingdom are governed by the Human Medicines Regulations (SI 2012 / 1916), as amended. Since** January 1, 2021, ~~and~~ **an** ~~formally entered~~ **applicant for the EU centralized procedure marketing authorization can no longer be established in the United Kingdom. As a result, since this date, companies established in the United Kingdom cannot use the EU centralized procedure and instead must follow one of the United Kingdom national authorization procedures or one of the remaining post- Brexit international cooperation procedures to obtain a marketing authorization to market products in the United Kingdom. All existing EU marketing authorizations for centrally authorized products were automatically converted or grandfathered** into ~~force~~ **United Kingdom marketing authorization, effective in Great Britain only, free of charge** on ~~May~~ **January** 1, 2021 **, unless the marketing authorization holder opted- out of this possibility. Northern Ireland currently remains within the scope of EU authorizations in relation to centrally authorized medicinal products. Accordingly, until the Windsor Framework is implemented in Northern Ireland on January 1, 2025, products falling within the scope of the EU centralized procedure can only be authorized through United Kingdom national authorization procedures in Great Britain. The MHRA has also introduced changes to national marketing authorization procedures. This includes introduction of procedures to prioritize access to new medicines that will benefit patients, including a 150- day assessment route, a rolling review procedure and the International Recognition Procedure. Since January 1, 2024, the MHRA may rely on the International Recognition Procedure, or IRP, when reviewing certain types of marketing authorization applications. This procedure is available for applicants for marketing authorization who have already received an authorization for the same product from a reference regulator. These include the FDA, the EMA, and national competent authorities of individual EEA countries. A positive opinion from the EMA and CHMP, or a positive end of procedure outcome from the mutual recognition or decentralized procedures are considered to be authorizations for the purposes of the IRP. There is no pre- marketing authorization orphan designation for medicinal products in the United Kingdom. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding marketing authorization application. The criteria are essentially the same as those in the EU, but have been tailored for the market. This includes**

the criterion that prevalence of the condition in Great Britain, rather than the EU, must not be more than five in 10, 000. Upon the grant of a marketing authorization with orphan status, the medicinal product will benefit from up to 10 years of market exclusivity from similar products in the approved orphan indication. The start of this market exclusivity period will be set from the date of first approval of the product in Great Britain . Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from European Union directives and regulations, Brexit has materially impacted and could continue to further impact, the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union ~~. For example, Great Britain is no longer covered by the centralized procedures for obtaining European Union- wide marketing and manufacturing authorizations from the EMA and a separate process for authorization of drug products is required in Great Britain~~ . Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would limit our ability to generate revenue and achieve and sustain profitability. In addition, while the Trade and Cooperation Agreement provides for the tariff- free trade of medicinal products between the United Kingdom and the European Union there are additional non- tariff costs to such trade which did not exist prior to Brexit. Furthermore, Brexit has reduced trade between the European Union and the United Kingdom and there are frequent delays in the transit of goods between the European Union and the United Kingdom. The ongoing impact of Brexit may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom or the European Union for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import / export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non- tariff barriers on us. Risks Related to the Manufacturing of our Product Candidates The manufacture of gene therapy products is technically complex and necessitates substantial expertise and capital investment. Production difficulties caused by unforeseen events may delay the availability of material for our clinical studies. We currently rely on third party contract manufacturing organizations, or CMOs, including Catalent, to manufacture our product candidates. We expect to rely on third party manufacturing organizations for our manufacturing needs for the foreseeable future. To date, our manufacturing partners have met our manufacturing requirements and quality standards for our program materials, and we expect that these organizations, primarily Catalent, will be capable of providing sufficient quantities of our program materials to meet anticipated clinical trial scale demands. While we believe that there are alternate sources of supply for our program materials that can satisfy our clinical and commercial requirements, identifying and establishing relationships with such sources, if necessary, would result in delays and additional costs, both of which could be significant. The manufacturers of pharmaceutical products must comply with strictly enforced cGMP requirements, state and federal regulations, as well as foreign requirements when applicable. Any failure of us or our CMOs to adhere to or document compliance to such regulatory requirements could lead to a delay or interruption in the availability of our program materials for clinical trials or enforcement action from the FDA, ~~EMA~~ **competent authorities of EU Member States** or foreign regulatory authorities. If we or our manufacturers were to fail to comply with the FDA, ~~EMA~~ **EU** or other regulatory authority **requirements** , it could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension **, variation** or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. Our potential future dependence upon others for the manufacture of our product candidates may also adversely affect our future profit margins and our ability to commercialize any product candidates that receive regulatory approval on a timely and competitive basis. Biological products are inherently difficult to manufacture. Although we believe that the manufacture of our product candidates may be simplified due to their shared raw materials and other similarities, we cannot be certain that this will be the case and we may be required to develop manufacturing methods that ultimately differ significantly between product candidates, which would require that we invest substantial time and capital to develop suitable manufacturing methods. Our program materials are manufactured using technically complex processes requiring specialized equipment and facilities, highly specific raw materials, cells, and reagents, and other production constraints. Our production process requires a number of highly specific raw materials, cells and reagents with limited suppliers. Even though we aim to have backup supplies of raw materials, cells and reagents whenever possible, we cannot be certain they will be sufficient if our primary sources are unavailable. A shortage of a critical raw material, cell line, or reagent, or a technical issue during manufacturing may lead to delays in clinical development or commercialization plans. We are particularly susceptible to any shortages, delays or our inability to obtain suitable AAV9 raw materials, given that all of our current and planned product candidates require this starting material. Any changes in the manufacturing of components of the raw materials we use could result in unanticipated or unfavorable effects in our manufacturing processes, resulting in delays. We and our contract manufacturers for AAV9 are subject to significant regulation with respect to manufacturing our products. The third- party manufacturing facilities on which we rely may have limited capacity or fail to meet the applicable stringent regulatory requirements. We currently have relationships with a limited number of suppliers for the manufacturing of plasmids and viruses, components of our product candidates. However, if we experience slowdowns or problems with our facility or those of our manufacturing partners and are unable to establish or scale our internal manufacturing capabilities, we will need to continue to contract with manufacturers that can produce the preclinical, clinical and commercial supply of our products. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to license such intellectual property rights on reasonable commercial terms or to transfer or sublicense the intellectual property rights we may have with respect to such activities. All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing CMOs for components of our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late- stage clinical trials in the European Union must be manufactured in accordance with cGMP. These regulations govern manufacturing

processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We are at an increased risk given that our product candidates have been and for the foreseeable future will be produced on the same manufacturing lines, which could, for example, lead to issues with cross- contamination. We or our CMOs must supply all necessary documentation in support of a BLA or MAA on a timely basis. Our facilities and quality systems and the facilities and quality systems of some or all of our third- party contractors must pass a pre- approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted, and they could put a hold on one or more of our clinical trials if the facilities of our contract development and manufacturing organizations, or CDMOs, do not pass such audit or inspections. If these facilities do not pass a pre- approval plant inspection, FDA approval of the products will not be granted. The regulatory authorities also may, at any time following approval of a product for sale, inspect or audit our manufacturing facilities or those of our third- party contractors **, including periodic unannounced inspections by the FDA, competent authorities of EU Member States or other comparable foreign regulatory authorities, to monitor and ensure compliance with cGMP** . If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and / or time- consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could harm our business. If we or any of our third- party manufacturers fail to maintain regulatory compliance, the FDA **or comparable foreign regulatory authority** can impose regulatory sanctions including, among other things, **shutdown of the third- party vendor or invalidation of drug product lots or processes, fines, injunctions, civil penalties, delays,** refusal to approve a pending application for a new drug product or biologic product, or revocation **, suspension or variation** of a pre- existing approval ~~. As a result~~ , **license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products, if approved, and significantly harm** our business, financial condition ~~and~~ **,** results of operations **and prospects** ~~may be harmed~~ . Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA and / or MAA supplement which could result in further delay. The regulatory ~~agencies~~ **authorities** may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully, if approved. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue. We depend on third- party suppliers for materials used in the manufacture of our product candidates, and the loss of these third- party suppliers or their inability to supply us with adequate materials could harm our business. We rely on third- party suppliers for certain materials and components required for the production of our product candidates. Our dependence on these third- party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability, and quality and delivery schedules. There is substantial demand and limited supply for certain of the raw materials used to manufacture gene therapy products. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors that 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 supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business. Any contamination or interruption in our manufacturing process, shortages of raw materials or failure of our suppliers of plasmids and viruses to deliver necessary components could result in delays in our clinical development or marketing schedules. Given the nature of gene therapy manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates proceed through preclinical studies to late- stage clinical trials towards potential 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 processes and product characteristics. Such changes carry the risk that they will not achieve our intended objectives. Any such 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 materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval **, or comparable foreign regulatory requirements** . 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 commence sales and generate revenue. In addition, we may be required to make significant changes to our upstream and downstream processes across our pipeline, which could delay the development of our future product candidates. Risks Related to the Commercialization of our Product Candidates Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third- party payors and others in the medical community necessary for commercial success. If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including: • the efficacy, safety and potential advantages compared to alternative treatments; • our ability to offer our products for sale at competitive prices; • the convenience and ease of administration compared to alternative treatments; • product labeling or product insert requirements of the FDA or foreign regulatory authorities, including any limitations or warnings contained in a product' s approved labeling, including any black box warning or REMS **or comparable foreign strategy** ; • the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments; • our ability to hire and retain a sales force in the United States; • the strength of marketing and distribution support; • the availability of third- party coverage and adequate reimbursement for TSHA- 102 ~~and TSHA- 120~~ and any other product candidates, once approved; • the prevalence and severity of any side effects; and • any restrictions on the use of our products together with other medications. Our potential therapeutic products involve introducing genetic material into a patient' s cells via intrathecal administration. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene regulation are unsafe, unethical or immoral, and consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products once approved. For example, in 2003, trials using early versions of murine gamma- retroviral vectors, which integrate with, and thereby alter, the host cell' s DNA, have led to several well- publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma- retroviral vectors, our product candidates use AAV9 viral vectors. Among the risks in any gene therapy product based on viral vectors are the risks of immunogenicity, elevated liver enzymes, and insertional oncogenesis. If any of our vectors demonstrate a similar effect we may decide or be required to halt or delay further clinical development of any product candidates that utilize that vector. Adverse events in our or others' clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical trials or in any clinical trials conducted by other companies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. In addition, for our regulated gene replacement therapy candidates that require that the expression of a therapeutic transgene be tightly regulated, such as TSHA- 102, we may inadvertently cause overexpression, which could lead to numerous issues, including safety and toxicity concerns. Furthermore, these regulatory gene replacement therapy candidates require the insertion of miRNA targets into the viral genome, which is a technology that to our knowledge is not present in any approved gene therapy products. If any such adverse events occur, commercialization of our product candidates or further advancement of our clinical trials could be halted or delayed, which would have a negative impact on our business and operations. If we are unable to establish sales, marketing and distribution capabilities for TSHA- 102 ~~and TSHA- 120~~ or any other product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved. We do not have sales or marketing infrastructure. To achieve commercial success for TSHA- 102 ~~, TSHA- 120,~~ or any other product candidate for which we may obtain marketing approval, we will need to establish a sales and marketing organization. In the future, we expect to build a focused sales and marketing infrastructure to market some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Factors that may inhibit our efforts to market our products on our own include: • our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel; • the inability of sales personnel to obtain access to physicians in order to educate physicians about our product candidates, once approved; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive

product lines; and • unforeseen costs and expenses associated with creating an independent sales and marketing organization. If we are unable to establish our own sales, marketing and distribution capabilities and are forced to enter into arrangements with, and rely on, third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we had developed such capabilities ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. The affected populations for our other product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates. We currently focus our research and product development on several indications that are orphan diseases. However, our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are estimates based on our knowledge and understanding of these diseases. These estimates may prove to be incorrect and new studies may further reduce the estimated incidence or prevalence of this disease. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our product candidate or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects. The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access and product pricing and reimbursement. Incidence and prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward- looking and speculative. The process we have used in developing an estimated incidence and prevalence range for the indications we are targeting has involved collating limited data from multiple sources. Accordingly, the incidence and prevalence estimates included in this Annual Report on Form 10- K should be viewed with caution. Further, the data and statistical information used in this Annual Report on Form 10- K, including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources. Drug development, particularly in the gene therapy field, is highly competitive and subject to rapid and significant technological advancements. As a significant unmet medical need exists in the neurology field, particularly for the treatment of neurodegenerative diseases, neurodevelopmental disorders and genetic epilepsies, there are several large and small pharmaceutical companies focused on delivering therapeutics for the treatment of these diseases. Further, it is likely that additional drugs will become available in the future for the treatment of our target indications. **Trofinetide was approved by the FDA in March 2023 for the treatment of Rett Syndrome.** We ~~believe that the majority of our programs will face limited competition as there are no approved disease- modifying therapies for the treatment of the GAN, Rett syndrome, or the other development programs in our pipeline. However, we~~ are aware that our competitors are developing product candidates for the treatment of diseases that our product candidates will target. With respect to TSHA- 102, we are aware that Neurogene has a clinical stage gene therapy program for the treatment of Rett syndrome. We are also aware that Alcyone Therapeutics, the Rett Syndrome Research Trust, Amicus Therapeutics, Shape Therapeutics and Sarepta Therapeutics have disclosed the existence of discovery- stage gene therapy programs for the treatment of Rett syndrome. Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries. Our current and potential future competitors may also have significantly more experience commercializing drugs, particularly gene therapy and other biological products, that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors. We will face competition from other drugs or from other non- drug products currently approved or that will be approved in the future in the neurology field, including for the treatment of diseases and disorders in the therapeutic categories we intend to target. Therefore, our ability to compete successfully will depend largely on our ability to: • develop and commercialize drugs that are superior to other products in the market; • demonstrate through our clinical trials that our product candidates are differentiated from existing and future therapies; • attract qualified scientific, product development and commercial personnel; • obtain patent or other proprietary protection for our medicines; • obtain required regulatory approvals; • obtain coverage and adequate reimbursement from, and negotiate competitive pricing with, third- party payors; and • successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any product candidate we develop. The inability to compete with existing or subsequently introduced drugs would have an adverse impact on our business, financial condition and prospects. In addition, the reimbursement structure of approved gene therapies by other companies could impact the anticipated reimbursement structure of our gene therapies, if approved, and our business, financial condition, results of operations and prospects. Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in- license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving regulatory and marketing approval for, or commercializing, drugs before we do, which would have an adverse impact on our business and results of operations. ~~Any product candidates for which we intend to seek approval as biologic~~ **Biologic** products may face competition sooner than anticipated. The Biologics Price Competition and Innovation Act, or BPCIA, created an abbreviated approval pathway for

biological products that are biosimilar to or interchangeable with an FDA- licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12- year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor' s own preclinical data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity and potency of their product. ~~The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have an adverse effect on the future commercial prospects for our biological products.~~ There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12- year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated ~~. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non- biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing~~ . If competitors are able to obtain marketing approval for biosimilars referencing our candidates, if approved, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. The success of our product candidates will depend significantly on coverage and adequate reimbursement or the willingness of patients to pay for these procedures. We believe our success depends on obtaining and maintaining coverage and adequate reimbursement for our product candidates, including TSHA- 102 for the treatment of Rett syndrome ~~and TSHA- 120 for the treatment of GAN~~ and the extent to which patients will be willing to pay out- of- pocket for such products, in the absence of reimbursement for all or part of the cost. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third- party payors, including government health care programs (e. g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations, and other organizations is essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor- by- payor basis. One payor' s determination to provide coverage for a drug product does not assure that other payors will also provide coverage, and adequate reimbursement. The principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U. S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Third- party payors determine which products and procedures they will cover and establish reimbursement levels. Even if a third- party payor covers a particular product or procedure, the resulting reimbursement payment rates may not be adequate. Patients who are treated in- office for a medical condition generally rely on third- party payors to reimburse all or part of the costs associated with the procedure, including costs associated with products used during the procedure, and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement. Physicians may be unlikely to offer procedures for such treatment if they are not covered by insurance and may be unlikely to purchase and use our product candidates, if approved, for our stated indications unless coverage is provided and reimbursement is adequate. In addition, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Reimbursement by a third- party payor may depend upon a number of factors, including the third- party payor' s determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost- effective; supported by peer- reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational. Further, increasing efforts by third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost- effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost- effective. If third- party payors do not consider a product to be cost- effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third- party payors in connection with the potential sale of any of our product candidates. Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to the treatments in which our products are used under any foreign reimbursement system. **The EU provides options for EU Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product, it may refuse to reimburse a product at the price set by the manufacturer or it may instead adopt a system of direct or indirect controls on the**

profitability of the company placing the medicinal product on the market. Many EU Member States also periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost- effectiveness of our products to other available therapies. This Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. Legislators, policymakers and healthcare insurance funds in the EU and the United Kingdom may continue to propose and implement cost- containing measures to keep healthcare costs down, particularly due to the financial strain that the COVID- 19 pandemic has placed on national healthcare systems of European countries. These measures could include limitations on the prices we would be able to charge for product candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third- party payors. Further, an increasing number of EU and other foreign countries use prices for medicinal products established in other countries as " reference prices " to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere. There can be no assurance that TSHA- 102 ~~, TSHA- 120,~~ or any other product candidate, if approved for sale in the United States or in other countries, will be considered medically reasonable and necessary, that it will be considered cost-effective by third- party payors, that coverage or an adequate level of reimbursement will be available or that reimbursement policies and practices in the United States and in foreign countries where our products are sold will not adversely affect our ability to sell our product candidates profitably, if they are approved for sale. Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates or drugs that we may develop; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial participants; • significant costs to defend the related litigation; • substantial monetary awards paid to trial participants or patients; • loss of revenue; • reduced resources of our management to pursue our business strategy; and • the inability to commercialize any products that we may develop. Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Risks Related to Our Dependence on Third Parties **We currently rely on our collaboration with UT Southwestern for our preclinical research and development programs, including for discovering, preclinically developing and conducting all IND- enabling studies for our lead product candidates and our near- term future pipeline. Failure or delay of UT Southwestern to fulfill all or part of its obligations to us under the agreement, a breakdown in collaboration between the parties or a complete or partial loss of this relationship would materially harm our business.** Our collaboration with UT Southwestern is critical to our business. We entered into the UT Southwestern Agreement with UT Southwestern to discover and develop certain AAV vector- based therapeutics, and the product candidates developed under such collaboration currently represent all of our pipeline and discovery programs. We currently rely ~~exclusively~~ on UT Southwestern for ~~all~~ **much** of our preclinical research and development capabilities, and in particular the UT Southwestern Gene Therapy Program under the direction of Drs. Steven Gray and Berge Minassian. Pursuant to the UT Southwestern Agreement, UT Southwestern is primarily responsible for discovery, preclinical development activities, including all IND- enabling non- clinical studies and research grade manufacturing, and other collaborative activities set forth in the plan for the funded research including leading interactions with FDA and other regulatory authorities. Either party has the right in certain circumstances to terminate the collaboration pursuant to the terms of the UT Southwestern Agreement. If UT Southwestern delays or fails to perform its obligations under the UT Southwestern Agreement, disagrees with our interpretation of the terms of the collaboration or our discovery plan or terminates our existing agreement, our pipeline of product candidates would be significantly adversely affected and our prospects will be materially harmed. The term of the research funding portion of the UT Southwestern Agreement, under which we have the ability to acquire exclusive rights to additional gene therapy products for rare, monogenic CNS indications, has been extended to extend research funding pursuant to sponsored research agreements on a program- by- program basis. UT Southwestern has also entered into collaborations with third parties, including certain of our competitors, addressing targets and disease indications outside the scope of our collaboration. As a result, UT Southwestern may have competing interests with respect to their priorities and resources. We may have disagreements with UT Southwestern with respect to the interpretation of the UT Southwestern Agreement, use of resources or otherwise that could cause our relationship with UT Southwestern to deteriorate. As a result, UT Southwestern may reduce their focus on, and resources allocated to, our programs, potentially delaying or terminating our ability to advance product candidates through preclinical studies. Additionally, if either of Dr. Gray or Dr. Minassian were to leave UT Southwestern or to otherwise no longer be meaningfully involved with us, our preclinical research and development capabilities may be substantially reduced. Further, under the UT Southwestern Agreement, UT Southwestern is primarily responsible for

prosecuting and maintaining our licensed intellectual property, and it may fail to properly prosecute, maintain or defend such intellectual property. In such event, if we are unable to otherwise maintain or defend such intellectual property, we could face the potential invalidation of the intellectual property or be subjected to litigation or arbitration, any of which would be time-consuming and expensive. To enforce the licensed intellectual property rights under the UT Southwestern Agreement, we will need to coordinate with UT Southwestern, which could slow down or hamper our ability to enforce our licensed intellectual property rights. In such event, we could face increased competition that could materially and adversely affect our business. We intend to rely on third parties to conduct a significant portion of our existing clinical trials and potential future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials. We have engaged CROs for our ongoing and planned clinical trials for TSHA- 102 ~~and TSHA- 120~~. We expect to continue to rely on third parties, including clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. Further, the performance of our CROs may also be interrupted by health epidemics, including due to travel restrictions, quarantine policies, heightened exposure of CRO staff who are healthcare providers to health epidemics or prioritization of resources toward a health epidemic. In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly. We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA **and comparable foreign regulatory** ~~requires~~ **require** us to comply with standards, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on ~~a~~ government- sponsored ~~database~~ **databases** , **such as** ClinicalTrials. gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, ~~EMA~~ **European Commission** or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. In addition, 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 **and comparable foreign regulatory authorities** . The FDA **or comparable foreign regulatory authority** may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA **or comparable foreign regulatory authority** may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA **or comparable foreign regulatory authority** and may ultimately lead to the denial of marketing approval of TSHA- 102 ~~, TSHA- 120,~~ or any other product candidates. We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue. We may seek collaborations with third parties for the development or commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates. We may seek third- party collaborators for the development and commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators for any such arrangements include regional and national pharmaceutical companies and biotechnology companies. If we enter into any additional such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates would pose the following

risks to us: • collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations; • collaborators may not perform their obligations as expected; • collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create 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; • we could grant exclusive rights to our collaborators that would prevent us from collaborating with others; • product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates; • a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products; • disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time- consuming and expensive; • collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation; • collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and • collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise 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. If any future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue. Risks Related to our Intellectual Property We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and product candidates ~~. As of February 16, 2023, we in-license two U. S. patents expiring in 2038- 2039, two foreign patents expiring in 2028, 8 pending Patent Cooperation Treaty, or PCT, applications, 63 pending foreign patent applications and 17 pending United States utility patent applications, which, if issued, are expected to expire between 2037 and 2043, without taking into account any possible patent term adjustment, regulatory extensions, or terminal disclaimers, and assuming payment of all annuity and / or maintenance fees~~ . We cannot offer any assurances about which of our patent applications will issue, the breadth of any resulting patent or whether any of the issued patents will be found invalid and unenforceable or will be threatened by third parties. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing and commercializing a product, including a biosimilar product that would be competitive with one or more of our product candidates. Furthermore, any successful challenge to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any of our product candidates. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. The patent prosecution process is expensive and time- consuming. We may not be able to prepare, file and prosecute all necessary or desirable patent applications at a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, depending on the terms of any future in- licenses to which we

may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in- licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. In addition to the protection provided by our patent estate, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not amenable to patent protection. Although we generally require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, or that our trade secrets and other confidential proprietary information will not be disclosed. Moreover, our competitors may independently develop knowledge, methods and know- how equivalent to our trade secrets. Competitors could purchase our products, if approved, and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, our agreements or security measures may be breached, and we may not have adequate remedies for any breach. Also, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA is considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA' s disclosure policies may change in the future. If we are unable to prevent material disclosure of the non- patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition. Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time, and if we do not obtain protection under the Hatch- Waxman Amendments and similar non- United States legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed. 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. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch- Waxman Amendments, and similar legislation in the European Union. The Hatch- Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced and could have a material adverse effect on our business. If we fail to comply with our obligations in our current and future intellectual property licenses with third parties, we could lose rights that are important to our business. We are heavily reliant upon licenses to certain patent rights and proprietary technology for the development of our product candidates, in particular the UT Southwestern Agreement and our license agreements with Queen' s University and Abeona. These license agreements impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations, our licensors may have the right to terminate our licenses, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in- license from such licensor and may face other penalties. Such an occurrence would materially adversely affect our business prospects. Licenses to additional third- party technology and materials that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition. Although we control the prosecution, maintenance and enforcement of the licensed and sublicensed intellectual property relating to our product candidates, we may require the cooperation of our licensors and any upstream licensor, which may not be forthcoming. Therefore, we cannot be certain that the prosecution, maintenance and enforcement of these patent rights will be in a manner consistent with the best interests of our business. If we or our licensor fail to maintain such patents, or if we or our licensor lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future. Further, if we fail to comply with our development obligations under our license agreements, we may lose our patent rights with respect to such agreement on a territory- by- territory basis, which would affect our patent rights worldwide. Termination of our current or any future license agreements would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose

our rights under these agreements, including our rights to important intellectual property or technology. Any of the foregoing could prevent us from commercializing our other product candidates, which could have a material adverse effect on our operating results and overall financial condition. In addition, intellectual property rights that we in- license in the future may be sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents. Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, and there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the United States. Furthermore, the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific, and factual issues. Changes in either patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. For example, on September 16, 2011, the Leahy- Smith America Invents Act, or the Leahy- Smith Act, was signed into law. The Leahy- Smith Act included a number of significant changes to United States patent law. These included provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent and Trademark Office, or USPTO, has developed new and untested regulations and procedures to govern the full implementation of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy- Smith Act, and in particular, the first to file provisions, became effective in March 2013. The Leahy- Smith Act has also introduced procedures making it easier for third parties to challenge issued patents, as well as to intervene in the prosecution of patent applications. Finally, the Leahy- Smith Act contained new statutory provisions that require the USPTO to issue new regulations for their implementation, and it may take the courts years to interpret the provisions of the new statute. It is too early to tell what, if any, impact the Leahy- Smith Act will have on the operation of our business and the protection and enforcement of our intellectual property. However, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents. Further, the United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the United States Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have owned or licensed or that we might obtain in the future. An inability to obtain, enforce, and defend patents covering our proprietary technologies would materially and adversely affect our business prospects and financial condition. Similarly, changes in patent laws and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we may obtain in the future. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. For example, if the issuance in a given country of a patent covering an invention is not followed by the issuance in other countries of patents covering the same invention, or if any judicial interpretation of the validity, enforceability or scope of the claims or the written description or enablement, in a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection. We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful. Competitors may infringe the patents for which we have applied. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. If we initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and / or unenforceable. In patent litigation in the United States, counterclaims alleging invalidity and / or unenforceability are common, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. In an infringement proceeding, a court may decide that the patent claims we are asserting are invalid and / or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent claims do not cover the technology in question. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, post grant review, inter partes review and equivalent proceedings in foreign jurisdictions (for example, opposition proceedings). Such proceedings could result in revocation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could have a material adverse impact on our business. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions

with respect to our patent applications. An unfavorable outcome could require us to cease using the related technology or force us to take a license under the patent rights of the prevailing party, if available. Furthermore, our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. We may be unsuccessful in licensing or acquiring intellectual property from third parties that may be required to develop and commercialize our product candidates. A third party may hold intellectual property, including patent rights that are important or necessary to the development and commercialization of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to acquire or obtain a license to such intellectual property from these third parties, and we may be unable to do so on commercially reasonable terms or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third- party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment 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. As our current and future product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We cannot provide any assurance that our current and future product candidates do not infringe other parties' patents or other proprietary rights, and competitors or other parties may assert that we infringe their proprietary rights in any event. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and future product candidates, including interference or derivation proceedings before the USPTO. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third- party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize TSHA- 102 ~~, TSHA- 120~~ or any future product candidates. In order to successfully challenge the validity of any such United States patent in federal court, we would need to overcome a presumption of validity. As this burden is high and requires us to present clear and convincing evidence as to the invalidity of any such United States patent claim, there is no assurance that a court of competent jurisdiction would agree with us and invalidate the claims of any such United States patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third- party patents or patent applications, or we may incorrectly conclude that a third- party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that one of our product candidates infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non- practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit. We are aware of issued patent or patents issued to REGENX that claim AAV vectors that have an AAV9 capsid serotype. If we commercialize any of our product candidates prior to the expiry of those patents in 2026 without a license, the patent owner could bring an action claiming infringement. If we are found to infringe a third party' s valid intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be non- exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Under certain circumstances, we could be forced, including by court orders, to cease commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for substantial monetary damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed the patent at issue. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in

our favor, could be substantial, and litigation would divert our management' s attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations. We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. We employ individuals who were previously employed at other biotechnology or biopharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our future patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees. We may be subject to claims challenging the inventorship or ownership of our future patents and other intellectual property. We may also be subject to claims that former employees, collaborators, or other third parties have an ownership interest in our patent applications, our future patents, or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self- executing or the assignment agreements may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. If we rely on third parties to manufacture or commercialize our product candidates, or if we collaborate with additional third parties for the development of such product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third- party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations. In addition, these agreements typically restrict the ability of our advisors, employees, third- party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know- how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. We may enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world. Filing and prosecuting patent applications and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as that in the United States or Europe. These products may compete with our product candidates, and our future patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. In addition, we may decide to abandon national and regional patent applications before they are granted. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the United States, but may issue as patents with claims of different scope or may even be refused in other jurisdictions. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology. While we intend to protect our

intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition from others in those jurisdictions. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States and Europe and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property rights, which could make it difficult for us to stop the infringement of our future patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our future patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing as patents, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. 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. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and / or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and / or applications and any patent rights we may obtain in the future. Furthermore, the USPTO and various non- United States government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse of a patent or patent application can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non- compliance can result in abandonment or lapse of the patents or patent applications, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market, which could have a material adverse effect on our business. Any trademarks we have obtained or may obtain may be infringed or otherwise violated, or successfully challenged, resulting in harm to our business. We expect to rely on trademarks as one means to distinguish our product candidates, if approved for marketing, from the drugs of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe or otherwise violate our trademarks and we may not have adequate resources to enforce our trademarks. Any of the foregoing events may have a material adverse effect on our business. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative: • others may be able to make products that are similar to or otherwise competitive with our product candidates but that are not covered by the claims of our current or future patents; • an in- license necessary for the manufacture, use, sale, offer for sale or importation of one or more of our product candidates may be terminated by the licensor; • we or future collaborators might not have been the first to make the inventions covered by our issued or future issued patents or our pending patent applications; • we or future collaborators might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that our pending patent applications will not lead to issued patents; • issued patents that we own or in- license may be held invalid or unenforceable as a result of legal challenges by our competitors; • issued patents that we own or in- license may not provide coverage for all aspects of our product candidates in all countries; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; and • the patents of others may have an adverse effect on our business. Should any of these events occur, they could significantly harm our business, results of operations and prospects. Risks Related to Legal and Regulatory Compliance Matters Our relationships with customers, healthcare providers, including physicians, and third- party payors are subject, directly or indirectly, to federal ~~and~~ **,** state **and foreign** healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. Healthcare providers, including physicians, and third- party payors in the United States and elsewhere will 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, principal investigators, consultants, customers and third- party payors subject us to various federal ~~and~~

, state **and foreign** fraud and abuse laws and other healthcare laws, including, without limitation **in the United States** , the federal Anti- Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government ~~and ,~~ the states **and foreign countries** in which we conduct or may conduct our business. The laws that will affect our operations include, but are not limited to: • the federal Anti- Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, or to induce, either the referral of an individual, or the purchase, lease, order or arrangement for or recommendation of the purchase, lease, order or arrangement for any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term " remuneration " has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, signed into law in 2010, provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act; • the federal civil and criminal false claims laws, including, without limitation, the federal False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes " any request or demand " for money or property presented to the United States federal government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non- reimbursable, uses; • the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third- party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on health plans, healthcare clearinghouses and certain healthcare providers, known as " covered entities ", and their respective HIPAA " business associates ", which are independent contractors that perform certain services for or on behalf of covered entities involving the use or disclosure of individually identifiable health information, as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions; • the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children' s Health Insurance Program, with specific exceptions, to report annually to CMS information related to: (i) payments or other " transfers of value'' made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, and (ii) ownership and investment interests held by physicians and their immediate family members; and • analogous state and foreign laws and regulations; state **and foreign** laws that require 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 foreign** laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign 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 **. • Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti- bribery laws of European countries, national sunshine rules, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment** . Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes,

regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid **, or comparable foreign programs** , additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management' s attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and / or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements. Even if we obtain regulatory approval for TSHA- 102 ~~, TSHA- 120,~~ or any future product candidates, they will remain subject to ongoing regulatory oversight. Even if we obtain any regulatory approval for TSHA- 102 ~~, TSHA- 120~~ , or any future product candidates, such product candidates, once approved, will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submitting of safety and other post- market information, among other things. Any regulatory approvals that we receive for TSHA- 102, ~~TSHA- 120,~~ or any future product candidates may also be subject to a REMS **, comparable foreign strategies** , limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post- marketing testing, including Phase 4 trials and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post- marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will further be required to immediately report any serious and unexpected adverse events and certain quality or production problems with our products to regulatory authorities along with other periodic reports. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will also have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drug products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product' s approved label. As such, we will not be allowed to promote our products for indications or uses for which they do not have approval, commonly known as off- label promotion. The holder of an approved BLA **or comparable foreign approval** must submit new or supplemental applications and obtain prior approval for certain changes to the approved product, product labeling, or manufacturing process. A company that is found to have improperly promoted off- label uses of their products may be subject to significant civil, criminal and administrative penalties. In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing. If we fail to comply with applicable regulatory requirements following approval of TSHA- 102 ~~, TSHA- 120,~~ or any future product candidates, a regulatory authority may: • issue an untitled letter or warning letter asserting that we are in violation of the law; • seek an injunction or impose administrative, civil or criminal penalties or monetary fines; • suspend **, vary** or withdraw regulatory approval; • suspend any ongoing clinical trials; • refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners; • restrict the marketing or manufacturing of the drug; • seize or detain the drug or otherwise require the withdrawal of the drug from the market; • refuse to permit the import or export of product candidates; or • refuse to allow us to enter into supply contracts, including government contracts. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize TSHA- 102 ~~, TSHA- 120~~ or any future product candidates and harm our business, financial condition, results of operations and prospects. Even if we obtain FDA or EMA approval any of our product candidates in the United States or European Union, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential. In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country- by- country basis regarding safety and efficacy. Approval by the FDA in the United States or the ~~EMA~~ **European Commission** in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in

international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized. Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations. In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post- approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and / or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the United States pharmaceutical industry ~~. The ACA, among other things: (i) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (ii) expanded the entities eligible for discounts under the 340B drug pricing program; (iii) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23. 1 % and 13 % of the average manufacturer price, or AMP, for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100 % of the AMP; (iv) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new eligibility categories for individuals with income at or below 133 % (as calculated, it constitutes 138 %) of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (v) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologies that are inhaled, infused, instilled, implanted or injected; (vi) introduced a new Medicare Part D coverage gap discount program in which manufacturers must now agree to offer 70 % point- of- sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer' s outpatient drugs to be covered under Medicare Part D (increased from 50 %, effective January 1, 2019, pursuant to the Bipartisan Budget Act of 2018); (vii) created a new Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (viii) established the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug ~~. There have been judicial, congressional, and executive branch challenges to certain aspects of the ACA, including efforts to repeal or replace certain aspects of the ACA. For example, on June 17, 2021, the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Prior to the U. S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. In addition, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how any additional healthcare reform measures of the Biden administration will impact the ACA and our business. Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2 % per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, will remain in effect until 2032, unless additional congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100 % of a drug' s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. ~~Congress is considering additional health reform measures. ~~Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Presidential executive orders, congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, in July 2021, the Biden administration released an executive order, " Promoting Competition in the American Economy, " with multiple provisions aimed at prescription drugs. In response to Biden' s executive order, on September 9, 2021, ~~the U. S. Department of Health and Human Services, or ~~HHS ~~,~~ released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (i) directs HHS to

negotiate the price of certain high- expenditure, single- source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated " maximum fair price " for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions ~~will~~ take effect progressively starting in fiscal year 2023 **. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations** , although ~~they~~ **the** ~~may be~~ **Medicare drug price negotiation program is currently** subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. ~~Further,~~ **In response to** the Biden administration ~~released an additional~~ **' s October 2022** executive order **,** on ~~October~~ **February** 14, ~~2022~~ **2023** , ~~directing~~ HHS **released** ~~to submit~~ a report **outlining** ~~on how the~~ **three** ~~Center for Medicare and Medicaid Innovation can be further leveraged to test~~ new models for **testing by the CMS Innovation Center which will be evaluated on their ability to** ~~lowering~~ **lower** ~~drug~~ **the** ~~costs~~ **cost** ~~for Medicare~~ **of drugs, promote accessibility,** and ~~Medicaid beneficiaries~~ **improve quality of care** . It is unclear whether **the models** ~~this executive order or similar policy initiatives~~ will be ~~implemented~~ **utilized in any health reform measures** in the future **. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march- in rights under the Bayh- Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework** . At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that these and 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 drug. 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 drugs. In addition, FDA **and comparable foreign regulatory** regulations and guidance may be revised or reinterpreted by the FDA **or the comparable foreign regulatory** in ways that may significantly affect our business and our products. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for TSHA- 102 ~~, TSHA- 120,~~ or any future product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require: • additional clinical trials to be conducted prior to obtaining approval; • changes to manufacturing methods; • recalls, replacements, or discontinuance of one or more of our products; and • additional recordkeeping **. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each EU Member State, leading to a single decision for each EU Member State. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment by all EU Member States concerned, and a separate assessment by each EU Member State with respect to specific requirements related to its own territory, including ethics rules. Each EU Member State' s decision is communicated to the sponsor via the centralized EU portal. Once the clinical trial approved, clinical study development may proceed. The CTR foresees a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials in relation to which application for approval was made on the basis of the Clinical Trials Directive before January 31, 2023, the Clinical Trials Directive will continue to apply on a transitional basis until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. The CTR will apply to clinical trials from an earlier date if the related clinical trial application was made on the basis of the CTR or if the clinical trial has already transitioned to the CTR framework before January 31, 2025. Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. In light of the entry into application of the CTR on January 31, 2022, we may be required to transition clinical trials for which we have obtained regulatory approvals in accordance with the CTD to the regulatory framework of the CTR. Transition of clinical trials governed by the CTD to the CTR will be required for clinical trials which will have at least one site active in the E. U. on January 30, 2025. A transitioning application would need to be submitted to the competent authorities of E. U. Member States through the Clinical Trials Information Systems and related regulatory approval obtained to continue the clinical trial past January 30, 2025. This would require financial, technical and human resources. If we are unable to transition our clinical trials in time, the conduct of those clinical trials may be negatively impacted. It is currently unclear to what extent the UK will seek to align its regulations with the EU in the future. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency, or MHRA, launched an eight- week consultation on reframing the UK legislation for clinical trials. The UK Government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will determine how closely the UK regulations will align with the CTR. Failure of the UK to closely align its regulations with the EU may have an effect**

on the cost of conducting clinical trials in the UK as opposed to other countries and / or make it harder to seek a marketing authorization for our product candidates on the basis of clinical trials conducted in the United Kingdom. In addition, on April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation. If adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity opportunities for our product candidates in the EU and make them open to generic or biosimilar competition earlier than is currently the case with a related reduction in reimbursement status. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, our development plans may be impacted . Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of TSHA- 102 ~~, TSHA- 120,~~ or other product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition, and results of operations. Disruptions at the FDA, the SEC and other government agencies **and regulatory authorities** caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA **and comparable foreign regulatory authorities** to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the U. S. Securities and Exchange Commission, or SEC, and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies **and comparable regulatory authorities** may also slow the time necessary for new drugs or biologics to be reviewed and / or approved by necessary government agencies **and regulatory authorities** , which would adversely affect our business. For example, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business **. We are subject to legal proceedings and claims from time to time that may seek material damages or otherwise may have a material adverse effect on our business. The costs we incur in defending ourselves or associated with settling any of these proceedings, as well as a material final judgment or decree against us, could materially adversely affect our financial condition. We are subject to legal proceedings and claims from time to time that may seek material damages or otherwise may have a material adverse effect on our business. For example, in January 2024, we were named a nominal defendant in a shareholder derivative lawsuit against certain of our current and former directors in the Court of Chancery of the State of Delaware. See " Item 3 — Legal Proceedings " and " Part II, Item 8, Note 13 — Commitments and Contingencies " in this Annual Report on Form 10- K for more information. This or any future litigation could result in substantial costs and diversion of management' s attention and resources, which could adversely impact our business. The costs we incur in defending ourselves or associated with settling such proceedings, as well as a material final judgment or decree against us, could materially adversely affect our financial condition** . Risks Related to Employee Matters and Managing our Growth Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel, and recent changes to our team might harm future operating results. We are highly dependent on the management, development, clinical, financial and business development expertise of our executive officers. Each of our executive officers may currently terminate their employment with us at any time. We do not maintain " key person " insurance for any of our executives or employees. In March 2022, as part of our strategic prioritization initiatives to improve operating efficiency, we reduced our headcount by approximately 35 %, and throughout 2022 and early 2023 we further reduced headcount, including the separations of our former Chief Executive Officer, Chief Medical Officer and Chief Development Officer. These reductions resulted in a year- over- year reduction in headcount of 63 % at December 31, 2022 as compared to December 31, 2021. As of December 31, ~~2022~~ **2023** , we had ~~65~~ **52** employees. As a result of our headcount reductions, we have engaged various outside consultants, principally in the areas of clinical development and clinical operations. Although we believe these employee transitions are in the best interest of our company and our stockholders, these transitions may result in the loss of personnel with deep institutional or technical knowledge. Further, the transition could potentially disrupt our operations and relationships with employees, suppliers and partners and due to added costs, operational inefficiencies, decreased employee morale and productivity and increased turnover. In addition, our competitors may seek to use these transitions and the related potential disruptions to gain a competitive advantage over us. Furthermore, these changes increase our dependency on the other members of our leadership team and clinical and preclinical operations teams that remain with us, who are not contractually obligated to remain employed with us and may leave at any time. Any such departure could be particularly disruptive and, to the extent we experience additional turnover, competition for top talent is high such that it may take some time to find a candidate that meets our requirements. Our future operating results depend substantially upon the continued service of our key personnel and in significant part upon our ability to attract and retain qualified management personnel. If we are unable to mitigate these or other similar risks, our business, results of operation and financial condition may be adversely affected. Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our development and

commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Such competition may increase due to the recent move by companies to offer a remote or hybrid work environment. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Further, we may experience employee turnover, consistent with high numbers of employee resignations across the broader American economy, that would have an adverse impact on our business strategy. New hires require significant training and, in most cases, take significant time before they achieve full productivity. New employees may not become as productive as we expect, and we may be unable to hire or retain sufficient numbers of qualified individuals. If we are unable to continue to attract and retain high quality personnel, motivate existing employees or maintain our corporate culture in a hybrid or remote work environment, particularly if we experience increased turnover, our ability to pursue our growth strategy will be limited. Our employees, independent contractors, consultants, collaborators, principal investigators, CROs, 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, collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct that violates FDA **or comparable foreign** regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA **or comparable foreign regulatory authority** , manufacturing standards, federal and state healthcare laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, 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 business conduct and ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws, and the curtailment or restructuring of our operations. Risks Related to Ownership of our Common Stock The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses. Our stock price may be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Specifically, from September 24, 2020, the date our stock began trading on Nasdaq, through ~~February 27~~ **March 1** , ~~2023~~ **2024** our stock price fluctuated from a low of $ 0. ~~91~~ **50** to a high of $ 33. 35 per share. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including: • the reporting of unfavorable preclinical results; • the commencement, enrollment or results of our clinical trials of TSHA- 102 ~~, TSHA- 120,~~ or any future clinical trials we may conduct, or changes in the development status of our product candidates; • any delay in our regulatory filings for TSHA- 102 ~~, TSHA- 120,~~ or any other product candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority' s review of such filings, including without limitation the FDA' s issuance of a " refusal to file " letter or a request for additional information; • an inability to obtain additional funding; • failure by us to comply with the terms of our Term Loan Agreement; • adverse results from, delays in or termination of clinical trials; • adverse regulatory decisions, including failure to receive regulatory approval of our product candidates; • unanticipated serious safety concerns related to the use of TSHA- 102 ~~, TSHA- 120,~~ or any other product candidate; • changes in financial estimates by us or by any equity research analysts who might cover our stock; • conditions or trends in our industry; • changes in the market valuations of similar companies; • reports of adverse events in other gene therapy products or clinical studies of such products; • stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry; • publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts; • announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures; • our relationships with our collaborators; • announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us; • investors' general perception of our company and our business; • recruitment or departure of key personnel; • overall performance of the equity markets; • trading volume of our common stock; • disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • significant lawsuits, including patent or stockholder litigation; • changes in the structure of

healthcare payment systems; • general political and economic conditions; and • other events or factors, many of which are beyond our control. The stock market in general, and the Nasdaq Global Market 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, ~~including very recently in connection with the ongoing COVID- 19 pandemic,~~ which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions, inflation and other adverse effects or developments ~~relating to the ongoing COVID- 19 pandemic~~ , may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this section, could have a significant and material adverse impact on the market price of our common stock. In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management' s attention and resources from our business. If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline. **Sales** ~~A significant portion~~ of ~~our total outstanding~~ **a substantial number of** shares **of our common stock in** ~~are restricted from immediate resale but may be sold into~~ the **public** market ~~in the near future. This~~ could cause the market price of our common stock to drop significantly, even if our business is doing well. Sales of a substantial number of shares of our common stock in the public market could occur at any time ~~. Additionally, the holders of an aggregate of approximately 17. 7 million shares of our common stock, or their transferees, will have rights~~ , subject to ~~some conditions, to require us to file one or more registration statements covering their~~ -- **the** ~~shares or to include their shares in registration~~ -- **restrictions and limitations described below** ~~statements that we may file for ourselves or other stockholders, at which time such shares will be freely tradable. 7, 266, 342 shares are subject to a lock- up pursuant to the terms of the Securities Purchase Agreement, which expires 180 days after October 24, 2022~~ . If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly **. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act in the case of our affiliates** . In addition, we have filed registration statements on Form S- 8 under the Securities Act of 1933, as amended, or the Securities Act, registering the issuance of shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S- 8 **are** ~~will be~~ available for sale in the public market subject to vesting arrangements and exercise of options and the restrictions of Rule 144 in the case of our affiliates. An active trading market for our common stock may not continue to be developed or sustained. Prior to our initial public offering, there was no public market for our common stock. Although our common stock is listed on The Nasdaq Global Market, an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares of our common stock at an attractive price or at all. Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result. There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10, 000, 000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders. Our charter documents also contain other provisions that could have an anti- takeover effect, including: • only one of our three classes of directors will be elected each year; • stockholders will not be entitled to remove directors other than by a 66 2 / 3 % vote and only for cause; • stockholders will not be permitted to take actions by written consent; • stockholders cannot call a special meeting of stockholders; and • stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings. In addition, we are subject to the anti- takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock. Concentration of ownership of our common stock among our ~~existing executive officers, directors and~~ principal stockholders may prevent new investors from influencing significant corporate decisions. Our ~~executive officers, directors and~~ current beneficial owners of 5 % or more of our common stock and their respective affiliates beneficially own a majority of our common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder

approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions. Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders. We are an " emerging growth company " and a " smaller reporting company " and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors. We are an " emerging growth company " as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including: • not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting; • not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements; • reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and • not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until December 31, 2025 or, if earlier, (i) the last day of the fiscal year in which we have total annual gross revenue of at least $ 1. 235 billion, (ii) the date on which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non- affiliates exceeds $ 700 million as of the prior June 30th, or (iii) the date on which we have issued more than $ 1. 0 billion in non- convertible debt during the prior three- year period. Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a " smaller reporting company, " which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We have broad discretion in the use our cash and cash equivalents. We have broad discretion over the use of our cash and cash equivalents. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Our failure to apply our cash and cash equivalents effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use our cash and cash equivalents. Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment. You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: • any derivative action or proceeding brought on our behalf; • any action asserting a breach of fiduciary duty; • any action asserting a claim against us arising under the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws; • any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our restated certificate or our amended and restated bylaws; • any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the state of Delaware; 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. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. These exclusive forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive- forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business. General Risks We are subject to stringent and ~~changing~~ **evolving** obligations related to data privacy and security. Our actual or perceived failure to

comply with such obligations could lead to regulatory investigations or actions; litigation **(including class claims) and mass arbitration demands** ; fines and penalties; disruptions of our business operations ~~,~~ **;** reputational harm ~~,~~ **; loss of revenue or profits;** and other adverse business impacts. In the ordinary course of business, we collect, receive, store, process, use, generate, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share **(collectively** , ~~or~~ Process **)** ~~or Processing,~~ personal data ~~,~~ **and** sensitive information, and other information necessary to operate our business, for legal and marketing purposes, and for other business- related purposes, such as information we collect about patients and healthcare providers in connection with clinical trials in the U. S. and abroad, proprietary and confidential business data, trade secrets, and intellectual property. Our data ~~processing~~ **Processing** activities ~~may~~ subject us to numerous federal, state, local, and ~~international~~ **foreign** laws, regulations, and guidance industry standards, external and internal **data** privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. The number and scope of which is changing, subject to differing applications and interpretations, and which may be inconsistent among jurisdictions, or in conflict with other rules, laws or Data Protection Obligations (as defined below). In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws. For example, the HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. ~~Additionally~~ **In the past few years, numerous U. S. states — including California, Virginia, Colorado, Connecticut, and Utah — have enacted comprehensive data privacy and security laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt- out of certain data Processing activities, such as targeted advertising, profiling, and automated decision- making. The exercise of these rights may impact our business and ability to provide our products and services. Certain states also impose stricter requirements for Processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example** , the California Consumer Privacy Act of 2018, ~~or~~ **as amended by** the **California Privacy Rights Act of 2020 (CPRA) (collectively,** CCPA **)** , applies to personal data of consumers, business representatives, and employees **who are California residents** , and requires businesses to provide specific disclosure in privacy notices and ~~affording~~ honor requests of California residents certain rights ~~related to their personal data to exercise certain privacy rights~~ . The CCPA allows for ~~civil penalties for noncompliance (~~ up to $ 7, 500 per **intentional** violation ~~)~~ and allows private litigants affected by certain data breaches to recover significant statutory damages. Although ~~the CCPA exempts some data Processed in the context of clinical trials, the CCPA increases compliance costs and potential liability with respect to other personal data we maintain about California residents. In addition, the California Privacy Rights Act of 2020, or the CPRA, effective January 1, 2023, expands the CCPA by establishing a new California Privacy Protection Agency to implement and enforce the CCPA, and adding a new right for individuals to correct their personal data. Other states have enacted data privacy and security laws. For example, Virginia passed its Consumer Data Protection Act, and Colorado passed the Colorado Privacy Act, both of which share similarities with, but also differ from, the CPRA and are effective in 2023. While~~ these states, like the CCPA, also exempt some data ~~processed~~ **Processed** in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely. Outside the United States, an increasing number of laws, regulations, and industry standards **govern** ~~apply to~~ data privacy and security. Our operations may be subject to increased scrutiny or attention from foreign data privacy and security authorities. Our clinical trial programs and research collaborations outside the United States may implicate foreign data privacy and security laws, including in Canada **, the UK** and Europe. The European Union' s General Data Protection Regulation **(** ~~, or~~ EU GDPR **)** , the United Kingdom' s General Data Protection Regulation **(** ~~, or~~ UK GDPR **)** , and Canada' s Personal Information Protection and Electronic Documents Act **(** ~~, or~~ PIPEDA **)** , and various related provincial laws, as well as Canada' s Anti- Spam Legislation **(** ~~, or~~ CASL **)** , may apply to our operations. **The** ~~For example, the~~ EU GDPR, and the UK GDPR, impose strict requirements for Processing the personal data of individuals located, respectively, within the European Economic Area **(** ~~, or the~~ EEA **)** , and the United Kingdom **(** ~~, or the~~ UK **)** . Under the ~~EU~~ GDPR, government regulators may impose temporary or definitive bans on data Processing, as well as fines up to 20 million euros **under EU GDPR, 17. 5 million pounds sterling under UK GDPR** or **, in each case,** 4 % of the annual global revenue, whichever is greater. Further, the law allows for private litigation related to Processing of personal data brought by classes of data subjects or consumer protection groups authorized by law to represent their interests. ~~The UK GDPR allows~~ **Our employees and personnel use generative artificial intelligence (AI) technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages. In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States** ~~for~~ **or** ~~similar penalties~~ **other countries** . Certain jurisdictions, including Europe **and the UK** , have enacted data localization laws and cross- border personal data transfers laws. For example, absent appropriate safeguards or other circumstances, the EU GDPR **and UK GDPR** generally restricts the transfer of personal data to countries outside of the EEA **and UK respectively** , such as the United States ~~, which the European Commission does not consider as providing an adequate level of personal data protection. The European Commission released a set of Standard Contractual Clauses that are designed to be a valid mechanism by which entities can transfer personal data out of the EEA to jurisdictions that the European Commission has not found to provide an adequate level of protection. Currently, these Standard Contractual clauses are a valid mechanism to transfer personal data outside of the EEA. The Standard Contractual Clauses, however, require parties that rely upon them to comply with additional obligations such as conducting transfer impact~~

~~assessments to determine whether additional security measures are necessary to protect the at- issue personal data. Moreover, due to potential legal challenges, there exists some uncertainty regarding whether the Standard Contractual Clauses will remain a valid mechanism for personal data transfers out of the EEA. In addition, laws in Switzerland and the UK similarly restrict personal data transfers outside of those jurisdictions to countries such as the U. S. that do not provide an adequate level of personal data protection~~ . Other jurisdictions have enacted or are considering similar cross- border personal data transfer laws and local personal data residency laws, any of which could increase the cost and complexity of doing business. ~~If~~ **Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA standard contractual clauses, the UK' s International Data Transfer Agreement / Addendum, and the EU- U. S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U. S.- based organizations who self- certify compliance and participate in the Framework), if** we cannot implement a valid compliance mechanism for cross- border personal data transfers, **or if the requirements for a legally- compliant transfer are too onerous,** we may face **adverse consequences, including interruption or degradation of our operations,** increased exposure to regulatory actions, substantial fines, and injunctions against Processing or transferring personal data from Europe or elsewhere. Inability to import personal data to the United States may significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties subject to European and other data protection laws or requiring us to increase our personal data Processing capabilities in Europe and / or elsewhere at significant expense **. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups** . Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the EU GDPR' s cross- border data transfer limitations. We are also subject to the terms of our **data** privacy and security policies, representations, certifications, standards, publications and frameworks, and contractual obligations to third parties related to **data** privacy, security and the Processing **of** personal data **(collectively** , ~~or~~ Data Protection Obligations **)** , including without limitation, operating rules and standards imposed by industry organizations. Data privacy and security issues worldwide are, and are likely to remain, uncertain for the foreseeable future. We strive to comply with applicable data privacy and security laws and Data Protection Obligations to the extent possible, but we may at times fail to do so, or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our personnel, partners or vendors do not comply with applicable data privacy and security laws and Data Protection Obligations. **We publish privacy policies, marketing materials and other statements, such as compliance with certain certifications or self- regulatory principles, regarding data privacy and security.** If **these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices,** we **may be subject to investigation, enforcement actions by regulators or other adverse consequences. If we or the third parties on which we rely** fail, or are perceived to have failed, to address or comply with applicable data privacy and security laws and Data Protection Obligations, such failure or perceived failure could: increase our compliance and operational costs; expose us to regulatory scrutiny, actions, fines and penalties; result in reputational harm; interrupt or stop clinical trials; result in litigation and liability; result in an inability to Process personal data or to operate in certain jurisdictions; cause a material adverse impact to business operations or financial results; result in imprisonment of company officials; and otherwise result in other material harm to our business. With applicable data privacy and security laws, and Data Protection Obligations imposing complex and burdensome obligations, and with substantial uncertainty over the interpretation and application of these requirements, we have faced and may face additional challenges in addressing and complying with them, and making necessary changes to our privacy policies and practices, and may incur material costs and expenses in an effort to do so, any of which could materially adversely affect our business operations and financial results, and may limit the adoption and use of, and reduce the overall demand for, our products, which could have an adverse impact on our business. If our, or our vendors', information technology systems or data is or were compromised, we could experience adverse ~~impacts~~ **consequences** resulting from such compromise, including, but not limited to **regulatory investigations or action; litigation; fines and penalties;** interruptions to our operations such as our clinical trials ~~,~~ **;** claims that we breached our data privacy and security ~~obligations,~~ **laws;** harm to our reputation **;** ~~, and~~ a loss of customers or sales **; and other adverse consequences** . In the ordinary course of our business, we, and the third parties upon which we rely, Process proprietary, confidential and sensitive information, including personal data (including health ~~information~~ **- related data**), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties. We ~~may use~~ **rely on** third- party service providers and ~~subprocessors~~ **technologies** to help us operate ~~our~~ **critical** business **systems** and **to** ~~engage in Processing~~ --- **Process** ~~on our behalf~~ **sensitive information in a variety of context, including, without limitation, cloud- based infrastructure, data center facilities, encryption and authentication technology, employee email, and other functions** . We ~~may~~ also share sensitive information with our partners or other third parties in conjunction with our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If we, our service providers, partners or other relevant third parties have experienced, or in the future experience, any security incident (s) that result in any data loss, deletion or destruction, unauthorized access to, loss of, unauthorized acquisition or disclosure of, or inadvertent exposure or disclosure of, personal data or sensitive information, or compromise related to the security, confidentiality, integrity or availability of our information technology, software, services, communications or data (or those of our service providers, partners or other relevant third parties) (~~"~~ collectively ~~",~~ Security Breach ~~"~~), it may have a material adverse effect on our business, including without limitation, regulatory investigations or enforcement actions, litigation, indemnity obligations, negative publicity and financial loss **, additional reporting requirements and / or oversight and restrictions on Processing sensitive information (including personal data)** . While we may be entitled to damages if our third- party service providers fail to satisfy their **data** privacy or

security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and could require us to incur substantial cost to recover or reproduce such data. Security Breaches and attendant consequences may **prevent or** cause customers to stop using our products, deter new customers for using our products, and otherwise negatively impact our ability to grow and operate our business. Cyberattacks, malicious internet- based activity and online and offline fraud and other similar activities are prevalent and continue to increase **and threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon which we rely** . These threats **are prevalent, continue to rise, are increasingly difficult to detect, and come from a variety of sources** come from a variety of sources, including traditional computer " hackers, " threat actors, personnel misconduct or error (employee theft or misuse), sophisticated nation- state and nation- state supported actors, " hacktivists, " organized criminal threat actors, and personnel (such as through theft or misuse). We ~~may be~~ **and the third- parties we rely are** subject to a variety of evolving threats, including but not limited to social engineering attacks (including through **deep fakes, which may be increasingly more difficult to identify as fake, and** phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of- service attacks **,** ~~(such as~~ credential stuffing ~~)~~, credential harvesting **, personnel misconduct or error** , ransomware attacks, supply- chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fire, flood **, attacks enhanced or facilitated by AI** , and other similar threats. Ransomware attacks, including those perpetrated by organized criminal threat actors, nation- states, and nation- state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting payments. Similarly, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third- party information technology systems that support us and our services. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation- state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, the third- party service providers upon which we rely, and our customers may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. The COVID- 19 pandemic and our remote workforce poses increased risks to our information technology systems and data, as more of our employees work from home, utilizing network connections outside our premises. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. We may be required to expend significant resources, fundamentally change our business activities **(including our clinical trial activities)** and practices, or modify our operations, including our clinical trial activities or information technology, in an effort to protect against Security Breaches and to mitigate, detect, and remediate actual and potential vulnerabilities. Applicable data privacy and security laws and Data Protection Obligations may require us to implement specific security measures or use industry- standard or reasonable measures to protect against Security Breaches. While we have implemented security measures designed to protect against Security Breaches, there can be no assurance that our security measures or those of our service providers, partners and other third parties will be effective in protecting against all Security Breaches and material adverse impacts that may arise from such breaches. The recovery systems, security protocols, network protection mechanisms and other security measures that we (and our third parties) have integrated into our platform, systems, networks and physical facilities, which are designed to protect against, detect and minimize Security Breaches, may not be adequate to prevent or detect service interruption, system failure or data loss. We have not always been able in the past and may be unable in the future to detect, anticipate, measure or prevent threats or techniques used to detect or exploit vulnerabilities in our (or our third parties') information technology, services, communications or software, or cause Security Breaches, because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after an incident has occurred. In addition, security researchers and other individuals have in the past and will continue in the future to actively search for and exploit actual and potential vulnerabilities in our (or our third parties') information technology and communications. While we take steps **designed** to detect and remediate vulnerabilities, ~~but~~ we may not be able to detect and remediate all vulnerabilities ~~because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated~~ in ~~nature~~ **a timely basis** . Therefore, such vulnerabilities could be exploited but may not be detected until after a ~~security~~ **Security** ~~incident~~ **Breach** has occurred. These vulnerabilities pose material risks to our business. We cannot be certain that we will be able to address any such vulnerabilities, in whole or part, and there may be delays in developing and deploying patches and other remedial measures to adequately address vulnerabilities. **Any of the previously identified or similar threats could cause a Security Breach or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A Security Breach or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our services.** Applicable data privacy and security laws and Data Protection Obligations may require us to notify relevant stakeholders of Security Breaches, including affected individuals, regulators and credit reporting agencies. Such disclosures are costly, and the disclosures or the failure to comply with such

requirements, could lead to material adverse impacts, including without limitation, negative publicity, a loss of confidence in our security measures or breach of contract claims. There can be no assurance **that our contracts contain a limitation of liability or** that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages if we fail to comply with ~~Applicable~~ **applicable** data privacy and security laws or Data Protection Obligations related to information security or Security Breaches. We may not have adequate insurance coverage in the event of a Security Breach. We cannot assure that our existing coverage will be adequate or otherwise protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or material adverse impacts arising out of our **data** privacy and security practices, Processing or Security Breaches we may experience, or that such coverage will continue to be available on acceptable terms or at all. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co- insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim. **In addition to experiencing a Security Breach** ~~Our contracts may not contain limitations of liability~~, **third parties may gather** ~~and even where they do~~, **collect,** ~~there can be no assurance that limitations of liability in our~~ **or infer sensitive information about** ~~contracts are sufficient to protect~~ us from ~~liabilities~~ **public sources**, ~~damages, or claims related to our~~ data ~~privacy~~ **brokers, or other means that reveals competitively sensitive details about our organization** and ~~security obligations~~ **could be used to undermine our competitive advantage or market position. Additionally, sensitive information could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel' s, or vendors' use of generative AI technologies**. If we fail, or are perceived to have failed, to address or comply with these data privacy and security **laws and Data Protection** ~~obligations~~ **Obligations**, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e. g., investigations, fines, penalties, audits, inspections and similar); litigation (including class- related claims); additional reporting requirements and / or oversight; bans on Processing personal data; and orders to destroy or not use personal data. Our business activities will be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti- bribery and anti- corruption laws. As we expand our business activities outside of the United States, including our clinical trial efforts, we will be subject to the FCPA and similar anti- bribery or anti- corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non- United States government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to 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. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non- United States governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers will be subject to regulation under the FCPA. We may engage third parties to sell our products sell our products outside the United States, to conduct clinical trials, and / or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition. We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them. We are subject to export control and import laws and regulations, including the U. S. Export Administration Regulations, U. S. Customs regulations and various economic and trade sanctions regulations administered by the U. S. Treasury Department' s Office of Foreign Assets Controls. Exports of our product candidates outside of the U. S. must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers. In addition, changes in our product candidates or changes in applicable export or import laws and regulations may create delays in the introduction, provision or sale of our product candidates in international markets, prevent customers from using our product candidates or, in some cases, prevent the export or import of our product candidates to certain countries, governments or persons altogether. Any limitation on our ability to export, provide or sell our product candidates could adversely affect our business, financial condition and results of operations. If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired. We are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes- Oxley Act of 2002, or the Sarbanes- Oxley Act, and the rules and regulations of The Nasdaq Stock Market. The

Sarbanes- Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in this report and future annual reports on Form 10- K, as required by Section 404 of the Sarbanes- Oxley Act. This requires that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to the year ended December 31, 2021, we have never been required to test our internal controls within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner. We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. 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 Nasdaq Stock Market, the SEC or other regulatory authorities. Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts. We are subject to taxation in more than one tax jurisdiction. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each such jurisdiction. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of newly enacted tax legislation, changes in the mix of our profitability from jurisdiction to jurisdiction, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in existing tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements. We might not be able to utilize a significant portion of our net operating loss carryforwards. We have generated and expect to continue to generate significant federal and state net operating loss, or NOL, carryforwards in the future. As of December 31, ~~2022~~ **2023**, there were federal and state NOLs of $ ~~216~~ **222**. ~~3~~ **1** million and $ ~~4~~ **11**. ~~5~~ **9** million respectively. **A portion of** ~~These~~ **these** NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Tax Cuts and Jobs, or the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, federal NOLs incurred in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain how various states will respond to the Tax Act and CARES Act. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an " ownership change, " which is generally defined as a greater than 50 % change, by value, in its equity ownership over a three- year period, the corporation' s ability to use its pre- change NOL carryforwards and other pre- change tax attributes to offset its post- change income or taxes may be limited. During ~~2022~~ **2023**, we performed a detailed analysis of historical and current Section 382 ownership ~~changes~~ **shifts** that may limit the utilization of NOL carryforwards. ~~Except for approximately~~ **None of our gross Federal NOLs are permanently limited. However, as a result of the ownership shift that occurred in August 2023,** $ ~~2~~ **27. 1 million of our research credits will expire and $ 217**. 9 million of ~~NOLs arising prior to~~ our **gross Federal** ~~initial public offering in September 2020, none of our~~ NOLs are ~~limited~~ **subject to an annual utilization limitation of $ 3. 1 million**. However, sales of our common stock by our existing stockholders, or additional sales of our common stock by us, could trigger additional limitations under Section 382 ~~and~~ **which could** have a material adverse effect on our results of operations in future years. New tax laws or regulations, changes to existing tax laws or regulations or changes in their application to us or our customers may have a material adverse effect on our business, cash flows, financial condition or results of operations. New tax laws, statutes, rules, regulations, directives, decrees or ordinances could be enacted at any time. Further, existing tax laws, statutes, rules, regulations, directives, decrees or ordinances could be interpreted, changed or modified. Any such enactment, interpretation, change or modification could adversely affect us, possibly with retroactive effect. For example, the ~~recently enacted~~ Inflation Reduction Act imposes, among other rules, a 15 % minimum tax on the book income of certain large corporations and a 1 % excise tax on certain corporate stock repurchases. In addition, for certain research and experimental, or R & E, expenses incurred in tax years beginning after December 31, 2021, the Tax Act requires the capitalization and amortization of such expenses over five years if incurred in the United States and fifteen years if incurred outside the United States, rather than deducting such expenses currently. Although there have been legislative proposals to repeal or defer the capitalization requirement, there can be no assurance that such requirement will be repealed, deferred or otherwise modified. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings and the deductibility of expenses under the Tax Act, as amended by the CARES Act or any future tax reform legislation, could have a material impact on the value of our deferred tax assets, result in significant one- time charges and increase our future U. S. tax expense. We have incurred and will continue to incur increased costs and demands upon management as a result of being a public company. As a public company listed in the United States, we have incurred and will continue to incur significant additional legal, accounting and other costs including the cost of director and officer liability insurance. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and the Nasdaq Stock Market, may increase legal and financial compliance costs and make some activities more time- consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided

by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management' s time and attention from revenue- generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed. Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management. **83**