Risk Factors Comparison 2024-03-13 to 2023-03-09 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with the other information included or incorporated by reference in this Annual Report on Form 10- K. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations **. Risks Related to the Merger The Merger may not be completed and the Merger Agreement may be terminated in accordance with its terms. The Merger is subject to a number of conditions that must be satisfied or waived, in each case, prior to the completion of the Merger, as specified in the Merger Agreement. These conditions to the completion of the Merger, some of which are beyond our control, may not be satisfied or waived in a timely manner or at all, and, accordingly, the Merger may be delayed or not completed. If the Merger is not completed, we are subject to the following risks: • if the Merger Agreement is terminated under specified circumstances, we may be required to pay Q32 a termination fee of $ 2. 4 million; • the price of our common stock may decline and could fluctuate significantly; and • costs related to the Merger, such as financial advisor, legal and accounting fees, which we estimate will total approximately $ 5. 6 million, which must be paid even if the Merger is not completed. If the Merger Agreement is terminated and our board of directors determines to seek another business combination, there can be no assurance that we will be able to find a partner with whom a business combination would yield greater benefits than the benefits to be provided under the Merger Agreement. If we and Q32 complete the Merger, the combined company will need to raise additional capital by issuing equity securities or additional debt or through licensing arrangements, which may cause significant dilution to the combined company' s stockholders or restrict the combined company' s operations. Additional financing may not be available to the combined company when it is needed or may not be available on favorable terms. To the extent that the combined company raises additional capital by issuing equity securities, such financing will cause additional dilution to all securityholders of the combined company, including our pre- Merger stockholders and Q32' s former securityholders. It is also possible that the terms of any new equity securities may have preferences over the combined company' s common stock. Any debt financing the combined company enters into may involve covenants that restrict its operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of the combined company' s assets, as well as prohibitions on its ability to create liens, pay dividends, redeem its stock or make investments. In addition, if the combined company raises additional funds through licensing arrangements, it may be necessary to grant licenses on terms that are not favorable to the combined company. Our stockholders may not realize a benefit from the Merger commensurate with the ownership dilution they will experience in connection with the Merger. If the combined company is unable to realize the full strategic and financial benefits currently anticipated from the Merger, our stockholders will have experienced substantial dilution of their ownership interests without receiving any commensurate benefit, or only receiving part of the commensurate benefit to the extent the combined company is able to realize only part of the strategic and financial benefits currently anticipated from the Merger. Certain provisions of the Merger Agreement may discourage third parties from submitting competing proposals, including proposals that may be superior to the transactions contemplated by the Merger Agreement. The terms of the Merger Agreement prohibit us from soliciting competing proposals or cooperating with persons making unsolicited takeover proposals, except in limited circumstances. In addition, if we terminate the Merger Agreement under specified circumstances, we may be required to pay Q32 a termination fee of $ 2. 4 million. This termination fee may discourage third parties from submitting competing proposals to us or our stockholders, and may cause our board of directors to be less inclined to recommend a competing proposal. Because the lack of a public market for Q32' s stock makes it difficult to evaluate the fair market value of Q32' s stock, we may pay more than the fair market value of Q32' s stock and / or the stockholders of Q32 may receive consideration in the Merger that is less than the fair market value of Q32' s stock. The outstanding Q32 common stock is privately held and is not traded in any public market. The lack of a public market makes it difficult to determine the fair market value of Q32' s stock. Because the percentage of our equity to be issued to Q32 stockholders was determined based on negotiations between the parties, it is possible that the value of our common stock to be received by Q32 stockholders will be less than the fair market value of Q32' s stock, or we may pay more than the aggregate fair market value for Q32' s stock. Stockholders could file lawsuits relating to the Merger. As of the date of this Annual Report on Form 10- K, there are no pending lawsuits challenging the Merger. However, potential plaintiffs may file lawsuits challenging the Merger. The outcome of any future litigation is uncertain. Such litigation, if not resolved, could prevent or delay consummation of the Merger and result in substantial costs to us, Q32, or the combined company, including any costs associated with the indemnification of directors and officers. One of the closing conditions is the absence of any order or legal requirement that restrains, enjoins, or otherwise prevents the consummation of the Merger. Therefore, if a plaintiff were successful in obtaining an injunction prohibiting the consummation of the Merger on the agreed- upon terms, then such injunction may prevent the Merger from being consummated, or from being consummated within the expected time frame** . Risks Related to Our Financial Position and Need for Additional Capital We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future. If we are unable to achieve and sustain profitability, the market value of our common stock

will likely decline. We may never achieve or maintain profitability. We are a clinical- stage genetic medicines company with a limited operating history. **Since inception, we have incurred significant operating losses. Our net losses for the year ended December 31, 2023 was $ 113. 0 million. As of December 31, 2023 and December 31, 2022, we had an accumulated deficit of $ 542. 1 million and $ 429. 1 million, respectively.** On March 10, 2022, we closed our transaction with OXB ~~Solutions~~ **(US) LLC** and recorded a gain of $ 131. 2 million on the sale of our manufacturing business ~~,~~ **which resulted in** which resulted in net income of $ 92. 1 million for the three months ended March 31, 2022 (see Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10- K for additional information regarding the OXB ~~Solutions~~ **(US) LLC** Transaction). ~~As of December 31, 2022 and December 31, 2021, we had an accumulated deficit of $ 429. 1 million and $ 424. 1 million, respectively. Since inception, we have incurred significant operating losses.~~ Our net ~~losses~~ **loss** for the ~~years~~ **year** ended December 31, 2022 **was** ~~and 2021 were~~ $ 5. 0 million ~~and $ 95. 8 million, respectively~~. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have **historically** devoted most of our financial resources to research and development, including our preclinical development activities. **In July 2023, we completed a review of our business and our board of directors approved a plan to explore, review and evaluate a range of potential strategic options available to us, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Based on the financing environment and our anticipated clinical development timeline, we stopped further development of our programs and reduced our workforce by 86 % to significantly reduce our ongoing operating costs as we evaluate strategic alternatives.** We **have incurred and expect to continue to incur costs and expenditures in connection with the process of evaluating our strategic alternatives and will continue to incur costs associated with operating as a public company. The process of continuing to evaluate strategic transactions may be costly, time- consuming and complex, and we may incur significant costs related to these processes, such as legal, accounting and advisory fees and expenses and other related charges. A considerable portion of these costs will be incurred regardless of whether any particular course of action is implemented or transaction is completed. Any such expenses will decrease the remaining cash available for use in our business. Should we resume development of our product candidates, we would** expect to continue to incur significant additional operating losses for the foreseeable future as we seek to advance product candidates through preclinical and clinical development, expand our research and development activities, develop new product candidates, complete clinical trials, seek regulatory approval and, if we receive **U. S. Food and Drug Administration, or** FDA **,** or foreign regulatory authorities approval, commercialize our products. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial. Because of the numerous risks and uncertainties associated with genetic medicines product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially if and as we: • continue our current research programs and our preclinical development of product candidates from our current research programs; • seek to identify, assess, acquire and / or develop additional research programs and additional product candidates; • initiate preclinical testing and clinical trials for any product candidates we identify and develop; • establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval; • maintain, expand and protect our intellectual property portfolio; • further develop our genetic medicines platform; • hire additional clinical, scientific and commercial personnel; • add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our operations as a public reporting company; • acquire or in- license other commercial products, product candidates and technologies; • make royalty, milestone or other payments under current and any future in- license agreements; and • further expand our Good Manufacturing Practices, or GMP, manufacturing capacity. Furthermore, **should we resume development of our product candidates,** our ability to successfully develop, commercialize and license our products and generate product revenue ~~is~~ **would be** subject to substantial additional risks and uncertainties. Each of our programs and product candidates will require additional preclinical and clinical development, potential regulatory approval in multiple jurisdictions, securing manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. These risks are further described under " — Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval " and " — Risks Related to Commercialization. " As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. The amount of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If we are unable to develop and commercialize one or more of our product candidates either alone or with collaborators, or if revenues from any product candidate that receives marketing approval are insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and then maintain profitability, the value of our equity securities will be materially and adversely affected. .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,debt financings,marketing and distribution arrangements and other collaborations,strategic alliances and licensing arrangements.As of December 31, ~~2023~~ **2022** ,we do not have any committed external source of funds.In addition,we may seek additional capital due to favorable market conditions or strategic considerations,even if we ~~believes~~ **believe** that we have sufficient funds for our current or future operating plans.To the extent that we raise additional capital through the sale of equity or convertible debt securities,including under our effective Registration Statement on Form S- 3,the ownership interests of our stockholders will be diluted,and the terms of these securities

may include liquidation or other preferences that adversely affect the rights of our common stockholders.Debt financing and preferred equity financing,if available,may involve agreements that include covenants limiting or restricting our ability to take specific actions,such as incurring additional debt,making capital expenditures or declaring dividends.If we ~~raises~~ **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 or grant licenses on terms that may not be favorable to us.If we are unable to raise additional funds through equity or debt financings when needed,we may be required to delay,limit,reduce or terminate our product development or future commercialization efforts ~~,should we resume development of our product candidates,~~ or grant rights to develop and market product candidates **that we would otherwise prefer to develop and market ourselves** We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to **continue** ~~complete the development and commercialization of~~ our **operations for more than twelve** ~~product candidates. We expect to spend substantial amounts~~ **months after** ~~to complete~~ the ~~development~~ **issuance date** of ~~, seek regulatory approvals for and commercialize~~ our ~~product candidates~~ **consolidated financial statements included elsewhere in this Annual Report on Form 10- K** . We will require additional capital, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates and any future product candidates **, should we resume such activities** . In addition, we may not be able to enter into any collaborations that will generate significant cash. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day- to- day activities ~~and harm our product candidate development efforts~~ . Based upon our current **projections** ~~operating plan~~ , we believe that our existing cash, cash equivalents, and short- term investments will enable us to fund our **operations for at least one year from the issuance date of our consolidated financial statements for the year ended December 31, 2023 included elsewhere in this Annual Report on Form 10- K. However, due to considerations of certain qualitative factors, including the discontinuation of all clinical trials and research activities, as well as our significant reduction in force of all but a few custodial employees, our management has concluded that there is substantial doubt regarding our ability to continue as a going concern for more than twelve months after the issuance date of our consolidated financial statements included elsewhere in this Annual Report on Form 10- K. Beyond that, we will need to raise additional capital in order to fund** operating expenses and capital expenditure requirements ~~into the fourth quarter of 2024, including, additional development activities related to our Phase 1 pheEDIT clinical trial with HMI- 103, our Phase 1 juMPStart clinical trial with HMI- 203, IND- enabling activities relating to HMI- 104, the continued optimization of our manufacturing processes and the expansion of our intellectual property portfolio~~ . This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. **In addition, our resource requirements could materially change depending on the outcome of our ongoing strategic alternative review process. As a result, we are unable to estimate the exact amount of our working capital requirements.** Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. **Should we resume** ~~Because the length of time and activities associated with successful~~ development of our product candidates **our** ~~and any future product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our~~ future funding requirements, both near and long- term, ~~will~~ **would** depend on many factors, including, but not limited to: • the initiation, progress, timing, costs and results of our planned clinical trials for our product candidates; • the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities; • the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights; • the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates; • the effect of competing technological and market developments; • the cost and timing of completion of commercial- scale manufacturing activities; • the costs of operating as a public company; • the extent to which we in- license or acquire other products and technologies; • the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products; and • the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale. We **maintain the majority of our cash and cash equivalents in accounts with major U. S. and multi- national financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintains our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. We** cannot be certain that additional funding will be available on acceptable terms, or at all. ~~Moreover~~ **For example** , ~~market~~ **the trading prices for our and other biopharmaceutical companies' stock have been highly** ~~volatility~~ **volatile as a** ~~resulting~~ **result** ~~from~~ **of macroeconomic conditions, developments in the industry and** the COVID- 19 pandemic **. As a result, we may face difficulties raising** ~~or other factors could also adversely impact our ability to access~~ capital ~~as~~ **through sales of our common stock** and ~~when needed~~ **any such sales may be on unfavorable terms** . If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of or product candidates or potentially discontinue operations . Raising additional capital may cause dilution..... otherwise prefer to develop and market ourselves . We have a limited operating history and no history of commercializing genetic medicine products, which may make it difficult to evaluate the prospects for our future viability. We were established and began operations in 2015. Our operations to date have been limited to financing

and staffing our company, developing our technology and identifying and developing our product candidates. We have not yet demonstrated an ability to successfully complete any clinical trials, including large- scale, pivotal clinical trials, obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes about six to ten years to develop a new drug from the time it enters Phase 1 clinical trials to when it is approved for treating patients, but in many cases, it may take longer. Consequently, **should we resume development of our product candidates,** predictions 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 genetic medicine products. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will eventually need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition. **We** ~~As we continue to build our business, we~~ expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance. ~~We are~~ **Should we resume development of our product candidates, we would be** heavily dependent on the success of our product candidates, and if none of our candidates receives regulatory approval or is not successfully commercialized, our business may be harmed. **We** ~~To date, we~~ have **historically** invested a significant portion of our efforts and financial resources in the development of our product candidates. Our future success and ability to generate product revenue is substantially dependent on our ability to successfully develop, obtain regulatory approval for and successfully commercialize our product candidates. We currently have no products that are approved for commercial sale and may never be able to develop marketable products **, and we have stopped development activities** . ~~We~~ **Should we resume development of our product candidates, we** expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to development of these candidates, which ~~will~~ **would** require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, securing manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we can generate any revenues from any commercial sales. Accordingly, our business ~~currently~~ **has historically** ~~depends~~ **depended** heavily on the successful development, regulatory approval and commercialization of our product candidates, which may never occur. Therefore, we cannot be certain that any of our product candidates ~~will~~ **would** be successful in ~~ongoing or~~ future clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval. Even if we receive approval to market any product candidate from the FDA or other regulatory authorities, we cannot be certain that our product candidates will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Additionally, the research, testing, manufacturing, labeling, approval, sale, marketing and distribution of genetic medicine products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market any product candidate in the United States until it receives approval of a Biologics License Application, or BLA from the FDA, or in any foreign countries until it receives the requisite approval from such countries. We have not submitted a BLA to the FDA or comparable applications to other regulatory authorities and do not expect to be in a position to do so for the foreseeable future. If any of our product candidates shows unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed. Further, competitors may be developing products with similar technology and may experience problems with their products that could identify problems that would potentially harm our business. We may not be successful in our efforts to identify additional product candidates. **Historically,** ~~Part~~ **part** of our strategy **involved, and to the extent such activities are resumed in the future may** ~~involves~~ **involve,** identifying novel product candidates. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also: • we may not be able to assemble sufficient resources to acquire or discover additional product candidates; • competitors may develop alternatives that render our potential product candidates obsolete or less attractive; • potential product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights; • potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance; • potential product candidates may not be effective in treating their targeted diseases; • the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable; • a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or • the regulatory pathway for a potential product candidate ~~is~~ **may be** too complex and difficult to navigate successfully or economically. In addition **, should we resume development of our product candidates** , we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify additional suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations. We ~~will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations. We will need to significantly expand our organization, and we may have difficulty identifying, hiring and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a~~

~~disproportionate amount of its attention away from our day- to- day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and / or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth. In addition, effective as of the OXB Solutions Transaction closing date, OXB Solutions incorporated Homology' s AAV manufacturing capabilities and is now operated by AAV manufacturing personnel formerly employed by Homology. We may not be able to effectively manage this transition and it could put additional strain on our personnel resources. See" Management' s Discussion and Analysis of Financial Condition and Results of Operations — Oxford Biomedica Solutions Transaction" in Item 7 of Part II to this Annual Report on Form 10- K. Many of the biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are unable to continue to attract and retain high- quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited. We~~ may be required to make significant payments in connection with our license agreement with the City of Hope. Under our license agreement with **the City of Hope, or** COH, we are subject to significant obligations, including payment obligations upon achievement of specified milestones and royalties on product sales, as well as other material obligations, including potential payments if we were to sublicense the COH technology to additional strategic collaborators. If these payments become due, we may not have sufficient funds available to meet our obligations or we may have to direct funds from other development efforts, and as a result, our development efforts may be materially harmed. ~~We~~ **Should we resume development of our product candidates, we** intend to identify and develop product candidates based on our novel genetic medicines platform, which makes it difficult to predict the time and cost of product candidate development. ~~No products that utilize gene editing technology have been approved in the United States or in Europe, and there~~ **There** have only been a limited number of human clinical trials involving a gene editing product candidate. Moreover, none of those trials has involved our nuclease- free gene editing technology, prior to our initiated Phase 1 pheEDIT clinical trial. In addition, there have been a limited number of gene therapy products approved in the United States or in Europe and none of these products have utilized our AAVHSC platform. We have **historically** concentrated our research and development efforts on our genetic medicines platform, which uses both nuclease- free gene editing and gene therapy technologies. Our future success depends on the successful development of this novel therapeutic approach. ~~To date, no product that utilizes gene editing has been approved in the United States or Europe.~~ There have been a limited number of clinical trials of gene editing technologies, ~~however no product candidates have been approved,~~ and, prior to our ~~recently initiated~~ Phase 1 pheEDIT clinical trial, none of these clinical trials involved product candidates that utilize our novel gene correction editing technology. Moreover, there have been a limited number of gene therapy products approved in the United States or in Europe and none of these products have utilized our AAVHSC platform. In addition, because our programs ~~are~~ **, prior to our pausing of further product development, were** all in the research, preclinical or early- clinical stage, we have not ~~yet~~ been able to fully assess safety in humans, and there may be long- term effects from treatment with any of our future product candidates that we cannot predict at this time. Any gene correction editing product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, it will be difficult for us to test our future product candidates in animal models for either safety or efficacy. Also, animal models may not exist for some of the diseases we expect to pursue **, should we resume development of our product candidates** . Our genetic medicines platform is based on a family of 15 proprietary AAVHSCs which we can deploy through a nuclease- free gene editing modality, gene therapy, or GTx- mAb, which is designed to produce antibodies throughout the body. All applications rely on the unique ability of our AAVHSCs to efficiently target multiple tissues in the body. The mechanism of action by which these vectors target particular tissues is still not completely understood. Therefore, it is difficult for us to determine that our vectors will be able to properly integrate corrective DNA in or deliver gene transfer constructs to enough tissue cells to reach therapeutic levels. ~~We~~ **Should we resume development of our product candidates, we** cannot be certain that our AAVHSCs will be able to meet safety and efficacy levels needed to be therapeutic in humans or that they will not cause significant adverse events or toxicities. Furthermore, studies conducted by a third party in non- human primates **, or NHPs,** suggest that intravenous delivery of certain AAV vectors at very high doses may result in severe toxicity of the dorsal root ganglion, or DRG. To date, we have not observed the severe DRG toxicities described in these publications after intravenous administration in **NHPs** ~~non- human primates~~ with our naturally occurring AAVHSC vectors, and we have not seen these toxicities in our product candidates. However, we cannot be certain that we will be able to avoid triggering toxicities in our future preclinical or clinical studies **we may conduct with our product candidates** . Any such results could impact our ability to develop a product candidate. 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 genetic medicines platform, or any similar or competitive gene therapy or gene editing platforms, will result in the identification, development, and regulatory approval of any medicines, or that other genetic medicine technologies will not be considered better or more attractive for the development of medicines. There can be no assurance that any development problems we experience in the future related to our genetic medicines platform 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 in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to commercial partners. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate **, should we resume development of our product candidates,** or commercializing any product

candidates we may develop on a timely or profitable basis, if at all. Because gene therapy and gene editing are novel and the regulatory landscape that governs any product candidates we may develop is uncertain and continues 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 **, to the extent we resume such activities** . Regulatory requirements governing products created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory authority may not be indicative of what any other regulatory authority may require for approval, and there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy products, cell therapy products and other products created with genome editing technology. For example, the FDA maintains the Office of Therapeutic Products within its Center for Biologics Evaluation and Research, or CBER, with responsibility for the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. **Should we resume development of our product candidates,** ~~These~~ **these** and other regulatory review agencies, committees and advisory groups and any requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. Additionally, under NIH Guidelines supervision of human gene transfer trials includes evaluation and assessment 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, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. In the European Union, or EU, the European Medicines Agency, or EMA, has a Committee for Advanced Therapies, or CAT, that, in conjunction with the Committee for ~~Human~~ Medicinal Products **for Human Use** , or CHMP, is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products, or ATMPs. ATMPs 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. The CAT' s opinion is considered by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT' s draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. In the EU, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant EU guidelines. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post- approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that our compliance with them is likely necessary to gain and maintain approval for any of our product candidates. In addition, the EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any of our gene therapy or genome editing product candidates, but that remains uncertain at this point. The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to evaluate 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 created with novel genome editing technology such as ours can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. ~~Since~~ **To the extent** we ~~are~~ **resume our activities** developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or comparable regulatory 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. This may be a particularly significant risk for many of the genetically defined diseases for which we may develop product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory authorities administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in statute or regulations or the interpretation of new available data by applicable regulatory agencies. Changes in applicable regulatory guidelines may lengthen the regulatory review process for our product candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such product candidates, or lead to significant post- approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA and other regulatory authorities to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Furthermore, regulatory action or private litigation

could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future product candidates. ~~As~~ **Should** we ~~advance~~ **resume development of our** product candidates, we ~~will~~ **would** be required to consult with these regulatory and advisory groups and comply with all applicable guidelines, rules and regulations. If we fail to do so, we may be required to delay or terminate development of such product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a product candidate to market could decrease our ability to generate sufficient product revenue to maintain our business. Clinical trials are expensive, time- consuming, difficult to design and implement, and involve an uncertain outcome. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. ~~The~~ **Should we resume development of our product candidates, the** results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biotechnology and genetic medicines industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Even if our current and future clinical trials are completed as planned, we cannot be certain that their results will establish the safety, purity, potency and / or effectiveness of any of our product candidates to the satisfaction of the FDA or other regulatory authorities, even if we believe that such trials were successful. To date, we have not completed any clinical trials for our product candidates. ~~We~~ **Should we resume development of our product candidates, we** may experience delays in conducting any clinical trials and we do not know whether planned clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to: • the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies; • obtaining regulatory approval to commence a trial; • reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • obtaining institutional review board, or IRB, and ethics committee approval or positive opinion at each site; • recruiting suitable patients to participate in a trial; • developing and validating the companion diagnostic to be used in a clinical trial, if applicable; • having patients complete a trial or return for post- treatment follow- up; • clinical sites deviating from trial protocol or dropping out of a trial; • addressing patient safety concerns that arise during the course of a trial; • adding a sufficient number of clinical trial sites; or • manufacturing sufficient quantities of product candidate for use in clinical trials. ~~We~~ **Should we resume development of our product candidates, 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 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 safety and / or efficacy data 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; • be subject to additional post- marketing testing requirements; or • have the product removed from the market after obtaining marketing approval. ~~In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.~~ We could encounter further delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Monitoring Committee, or DMC, for such trial or by the FDA 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 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. Furthermore, we may rely on CROs and clinical trial sites to ensure the proper and timely conduct of clinical trials and while we would have agreements governing their committed activities, we would have limited influence over their actual performance, as described in " — Risks Related to Our Dependence on Third Parties. " ~~All~~ **To the extent we were to resume such activities,**

all of our product candidates ~~will~~ **would** require extensive clinical testing before we ~~are~~ **would be** prepared to submit a BLA or similar applications seeking regulatory approval. We cannot predict with any certainty if or when we might complete the development of any of our product candidate and submit a BLA or similar applications or whether any such BLA or similar applications will be approved by the FDA or comparable foreign authorities. We may seek feedback from the FDA or other regulatory authorities on our clinical development program, and the FDA 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. 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. 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. In addition, the FDA' s and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in **the** EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state **in which the clinical trial takes place** , to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application ~~to all member states concerned~~ **for multi- center trials** . The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR ~~foresees~~ **provides for** a three- year transition period ~~. The extent to which ongoing and new clinical trials will be governed by the CTR varies~~ . Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said **Clinical** ~~Directive~~ **TrialDirective** until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third- party service providers, such as clinical research organizations, or CROs, may impact our developments plans. It is currently unclear to what extent the United Kingdom, or UK, will seek to align its regulations with the EU. 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 Regulatory Agency, or MHRA, launched an eight- week consultation on reframing the UK legislation for clinical trials ~~. The consultation closed on March 14 2022 and~~ **with the** ~~aims~~ **aim** 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 ~~outcome of~~ **UK Government published its response to** the consultation is **on March 21, 2023 confirming that it would** ~~being~~ **bring forward changes to the legislation. These resulting legislative amendments will be** closely watched and will determine ~~whether~~ **how closely** the UK ~~chooses to~~ **regulations are** ~~align~~ **aligned** with the CTR ~~or diverge from it to maintain regulatory flexibility~~ . Under the terms of the Protocol on Ireland / Northern Ireland, provisions of the CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products apply in Northern Ireland. **On February 27, 2023, the UK Government and the European Commission reached a political agreement on the " Windsor Framework " which will revise the Protocol on Ireland / Northern Ireland in order to address some of the perceived shortcomings in its operation. Once implemented, this may have further impact on the application of the CTR in Northern Ireland.** A decision by the UK Government not to closely align ~~its regulations~~ **any new legislation** with the new approach adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be **adversely** impacted. Adverse public perception of genetic medicine, and gene editing in particular, may negatively impact the length of time required to advance our product candidates through clinical trials **should we resume development of our product candidates** , including the pace at which we advance patient enrollment, and potential regulatory approval of, or demand for, our potential products. Some of our ~~potential~~ therapeutic ~~products~~ **candidates** ~~involve~~ **involved** editing the human genome. ~~The~~ **If we resume the development of our product candidates in the future, the** clinical and commercial success of ~~our~~ **such** potential products ~~will~~ **would** depend in part on public acceptance of the use of gene editing and gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene editing 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. In addition, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2015, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work

prompted calls for a moratorium or other types of restrictions on gene editing of human eggs, sperm, and embryos. The Alliance for Regenerative Medicine in Washington, D. C. has called for a voluntary moratorium on the use of gene editing technologies in research that involved altering human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of gene editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey- Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Research on embryos is more tightly controlled in many other European countries. Although we do not use our technologies to edit human embryos or the human germline, **should we resume development of our product candidates,** such public debate about the use of gene editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene therapy or gene editing technologies, even if not ultimately attributable to product candidates we may discover and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, a decrease in demand for any such product candidates and a suspension or withdrawal of approval by regulatory authorities of our product candidates. A Breakthrough Therapy Designation from the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval. ~~We~~ **Should we resume development of our product candidates, we** may seek a Breakthrough Therapy Designation for our product candidates if the clinical data support such a designation for one or more product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug, or biologic in our case, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Biologics designated as breakthrough therapies by the FDA may also be eligible for priority review and rolling review of a BLA, if the relevant criteria are met. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under non- expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. A Fast Track Designation from the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval. On May 1, 2019, we received Fast Track Designation for HMI- 102 for the prevention or treatment of neurocognitive defects due to phenylalanine hydroxylase deficiency through normalization of circulating phenylalanine levels, and on October 25, 2021, we received Fast Track Designation for HMI- 103 for the treatment of neurocognitive and neuropsychiatric manifestations of PKU secondary to phenylalanine hydroxylase deficiency. ~~We intend to~~ **Should resume development of our product candidates, we may** seek such designation for some or all of our other product candidates. If a drug or biologic, in our case, is intended for the treatment of a serious or life- threatening condition and the biologic demonstrates the potential to address unmet medical needs for this condition, the biologic sponsor may **also** apply for FDA Fast Track Designation. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many biologics that have received Fast Track Designation have failed to obtain approval. ~~We~~ **In the future, we** may seek EMA PRIME designation or apply for other expedited regulatory pathways, designations, schemes or tools in the EU or UK for one or more of our product candidates, which we may not receive. Such designations may not lead to a faster development or regulatory review or approval process and do not increase the likelihood that our product candidates will receive marketing authorization. ~~We~~ **In the future, we** may seek EMA PRIME (Priority Medicines) designation or other designations, schemes or tools for one or more of our product candidates. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives

similar to the Breakthrough Therapy and Fast- Track designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA' s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. Even if we believe one of our product candidates is eligible for PRIME, the EMA may disagree and instead determine not to make such designation. The EMA PRIME scheme or other schemes, designations, or tools, even if obtained or used for any of our product candidates may not lead to a faster development, regulatory review or approval process compared to therapies considered for approval under conventional procedures and do not assure ultimate approval. In addition, even if one or more of our product candidates is eligible to the PRIME scheme, the EMA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for review or approval will not be shortened. Product developers that benefit from PRIME designation may be eligible for accelerated assessment (in 150 days instead of 210 days), which may be granted for medicinal products of major interest from a public health perspective or that target an unmet medical need, but this is not guaranteed. We may equally pursue some of the post- Brexit ~~UK~~ MHRA procedures to prioritize access to new medicines that will benefit patients, such as a 150- day assessment, a rolling review procedure and an innovative licensing and access pathway, or ILAP. ILAP aims to accelerate the time to market and to facilitate patient access to medicines, including new chemical entities, biological medicines, new indications and repurposed medicines. To benefit from ILAP, we must first apply to the MHRA for an innovation passport **. An innovation passport allows for enhanced engagement with the MHRA and its partner agencies. Once an innovation passport has been granted, the next step in the pathway is the preparation of a target development profile, or TDP, document by the MHRA and its partner agencies. The TDP sets out the regulatory and development milestones, identifies potential pitfalls and creates a roadmap to achieving early patient access in the UK** . Product developers that benefit from ILAP will be provided with advice on clinical trial design to ensure optimal data generation for both regulatory approval and health technology appraisal. The competent regulatory authorities in the EU and the UK have broad discretion whether to grant access to the aforementioned schemes and designations, and even if we were to be eligible for some of these procedures, we may not experience a faster development process, review or authorization compared to conventional procedures. Moreover, the removal or threat of removal of such designation may create uncertainty or delay in the clinical development of our product candidates and threaten the commercialization prospects of our product candidates, if approved. Such an occurrence could materially impact our business, financial condition and results of operations. ~~We~~ **Should we resume development of our product candidates, we** may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways or similar expedited approval pathways outside the United States. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA or similar expedited approval pathways by foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post- marketing requirements, the FDA or foreign regulatory authorities may seek to withdraw accelerated approval or similar expedited approval. ~~We~~ **To the extent we resume development of our product candidates, we** may in the future seek an accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a drug or biologic over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor' s agreement to conduct, in a diligent manner, confirmatory studies to verity and describe the drug or biologic' s predicted clinical benefit. ~~If~~ **Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post- approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis, if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if** confirmatory studies fail to confirm such clinical benefit ~~or if the sponsor fails to conduct such studies in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, President Biden signed an omnibus appropriations bill to fund the U. S. government through fiscal year 2023. Included in the omnibus bill is the Food and Drug Omnibus Reform Act of 2022, which among other things, introduced reforms intended to expand the FDA' s ability to regulate products receiving accelerated approval, including by increasing the FDA' s oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear~~ . In the EU, a " conditional " marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is

subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a " standard " marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed. Furthermore, marketing authorizations may also be granted " under exceptional circumstances " when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to the introduction of specific procedures. This may arise when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This type of marketing authorization is close to a conditional marketing authorization as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a marketing authorization. However, unlike a conditional marketing authorization, the applicant does not have to provide the missing data and will never have to. Although a marketing authorization " under exceptional circumstances " is granted definitively, the risk- benefit balance of the medicinal product is reviewed annually and the marketing authorization may be withdrawn where the risk- benefit ratio is no longer favorable. Prior to seeking accelerated approval or similar expedited approval for any of our product candidates, **should** we ~~intend to~~ **resume development of our product candidates, we may** seek feedback from the FDA or other comparable regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval or similar expedited approval. Furthermore, if we decide to submit an application for accelerated approval or similar expedited approval, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate **or make commercialization unfeasible** , **and** ~~if any,~~ could increase the cost of development of such product candidate and could harm our competitive position in the marketplace. We **may** ~~have received orphan drug designation for HMI- 102, HMI- 103, HMI- 202 and HMI- 203, and we intend to~~ seek orphan drug designation for our ~~other~~ product candidates **should we resume our development activities in the future** , but any orphan drug designations we **may** receive may not confer marketing exclusivity or other expected benefits ~~. We have received orphan drug designation for HMI- 102 and HMI- 103 in the United States and the EU for the use of AAVHSC15 expressing PAH for the treatment of PAH deficiency, for HMI- 202 in the United States and EU for the use of AAVHSC15 expressing human arylsulfatase A for the treatment of metachromatic leukodystrophy, or MLD and for HMI- 203 in the United States and the EU for the use of AAVHSC15 expressing human iduronate 2- sulfatase for the treatment of mucopolysaccharidosis type II (Hunter syndrome)~~ . In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user- fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full BLA, to market the same drug for the same disease or condition for seven years, except in limited circumstances. The applicable exclusivity period is ten years in the EU. The European exclusivity period can be reduced to six years if, at the end of the fifth year, a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. **In the future,** ~~Even~~ **even** if we, or any ~~future~~ **prospective** collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan- designated disease or condition due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for a disease or condition broader than the orphan- designated disease or condition or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same disease or condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same disease or condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process, nor does it prevent competitors from obtaining approval of the same product candidate as ours for diseases or conditions other than those in which we have been granted orphan drug designation. The same principles are valid for the EU as well. ~~We have received rare pediatric disease designation for HMI- 202, and we may seek rare pediatric disease designation for our other product candidates, however, there is no guarantee that we will obtain such designation, and even if we do, there is no guarantee that FDA approval will result in a priority review voucher. In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a " rare pediatric disease " that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another~~

~~sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U. S. within one year following the date of approval. We have received rare pediatric disease designation for HMI- 202 for the treatment of MLD, and we may seek rare pediatric disease designation for our other product candidates; however, we may not be able to obtain such designation. If we are able to obtain rare pediatric disease designation for our other product candidates, there is no guarantee that we will be able to obtain a priority review voucher, even if the designated product candidate is approved by the FDA. Moreover, Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Specifically, the FDA may not award the voucher to sponsors of marketing applications unless either (i) the drug has received rare pediatric disease designation as of September 30, 2024, and is then approved by the FDA no later than September 30, 2026; or (ii) Congress reauthorizes the program. Even though we received rare pediatric disease designation for HMI- 202 by the current statutory deadline of September 30, 2024, we may not receive the voucher if we do not obtain approval by September 30, 2026. Even if legislation is enacted that extends the date by which approval of the rare pediatric disease- designated drug must obtain approval to receive a priority review voucher, we may not obtain approval by that date, and even if we do, we may not obtain a priority review voucher.~~ A Regenerative Medicine Advanced Therapy designation from the FDA, or Advanced Therapy Medicinal Product classification by the EMA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval. ~~We~~ **Should we resume development of our product candidates, we** may seek a Regenerative Medicine Advanced Therapy, or RMAT, designation for HMI- 102 or our ~~other~~ product candidates. In 2017, the FDA established the RMAT designation as part of its implementation of the 21st Century Cures Act. An investigational drug is eligible for RMAT designation if: (1) it meets the definition of a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious disease or condition; and (3) preliminary clinical evidence indicates that the investigational drug has the potential to address unmet medical needs for such disease or condition. In a February 2019 final guidance, the FDA also stated that certain gene therapies that lead to a sustained effect on cells or tissues may meet the definition of a regenerative medicine therapy. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review of BLAs and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long- term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites, as appropriate. RMAT- designated product candidates that receive accelerated approval may, as appropriate, fulfill their post- approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post- approval monitoring of all patients treated with such therapy prior to approval of the therapy. RMAT designation does not change the standards for product approval, and there is no assurance that such designation or eligibility for such designation will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the RMAT designation. Additionally, RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges. In the EU, a specific framework has been implemented for ATMPs to facilitate their access to the EU market. An ATMP can be classified into three main types of medicinal products: (i) gene therapy medicinal products containing genes that lead to a therapeutic, prophylactic or diagnostic effect, (ii) somatic- cell therapy medicinal products containing cells or tissues that have been manipulated to change their biological characteristics or cells or tissues not intended to be used for the same essential functions in the body which can be used to cure, diagnose or prevent diseases, and (iii) tissue- engineered products containing cells or tissues that have been modified so they can be used to repair, regenerate or replace human tissue. Companies developing product candidates may seek a scientific recommendation from the EMA' s CAT on ATMP classification. This optional procedure allows applicants to clarify whether a given product candidate based on genes, cells or tissues meets the scientific criteria which define ATMPs, in order to address, as early as possible, questions of borderline with other areas, which may arise as science develops. ATMP classification recommendation is adopted by the EMA' s CAT, after consultation with the EC. The EMA offers a range of advisory services and incentives to support the development of ATMPs such as contribution of the CAT' s members in the discussion of the scientific advice and fee waivers. Similarly to RMAT designation, ATMP classification in the EU does not change the standards for product approval, and there is no assurance that such classification will result in expedited review or approval. Our contract manufacturers, including Oxford Biomedica ~~Solutions~~ **(US)** LLC, are subject to significant regulation with respect to manufacturing our **former** product candidates. The manufacturing facilities ~~on~~ which we **have historically and may in the future** rely may not meet or continue to meet regulatory requirements, as applicable and as imposed to date, and have limited capacity. ~~We currently~~ **Historically, we** have **had** relationships with a limited number of suppliers for the manufacturing of our viral vectors and product candidates. In March 2022, we closed an agreement with Oxford to establish a new AAV vector manufacturing company, Oxford Biomedica ~~Solutions~~ **(US)** LLC, that incorporates our proven' plug and play' process development and manufacturing platform, as well as our experienced team and high- quality GMP vector production capabilities that we built and ~~have~~ operated since 2019. The related transactions closed on March 10, 2022. 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 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 studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late- stage clinical studies must be manufactured in accordance with ~~cGMP~~ - **GMP** or similar

requirements outside the United States. 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. Our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA' s current good laboratory practices, or GLP, and GMP regulations enforced by the FDA through its facilities inspection program. Similar requirements apply in foreign jurisdictions. Some of our contract manufacturers have not produced a commercially- approved product and therefore have not obtained the requisite FDA and foreign regulatory approvals to do so. 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. If these facilities do not pass a pre- approval plant inspection, FDA or foreign regulatory authorities approval of the products will not be granted. The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third- party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and / or time- consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business. If our third- party manufacturers fail to maintain regulatory compliance, the FDA or other regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre- existing approval. As a result, our business, financial condition and results of operations may be materially 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 supplement and / or marketing authorization application supplement which could result in further delay. The regulatory agencies 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 studies, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue. If we **resume development of our product candidates and** encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. ~~The~~ **Should we resume development of our product candidates, the** timely completion of clinical trials **would** ~~in accordance with their protocols depends~~ **depend** , among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. The enrollment of patients depends on many factors, including: • the patient eligibility criteria defined in the protocol; • the size of the patient population required for analysis of the trial' s primary endpoints; • the proximity of patients to study sites; • the design of the trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating; • our ability to obtain and maintain patient consents; and • the risk that patients enrolled in clinical trials will drop out of the trials before completion. In addition, **should we resume development of our product candidates,** our clinical trials ~~will~~ **would** compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition ~~will~~ **would** reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates, or could render further development impossible. Our product candidates have caused and may in the future cause serious adverse events or undesirable side effects or have other properties which may delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if any. Serious adverse events or undesirable side effects caused by our product candidates have caused, and could in the future cause, us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, toxicities or unexpected characteristics, including death. A significant risk in any gene editing product is that the edit will be " off- target " (or " on- target, " but unwanted) and cause serious adverse events, undesirable side effects, toxicities or unexpected characteristics. For example, off- target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off- target cut events, DNA from such repair template could be integrated into the genome at an

unintended site, potentially disrupting another important gene or genomic element. We cannot be certain that off- target editing will not occur in any of our planned or future clinical studies. There is also the potential risk of delayed adverse events following exposure to gene editing and / or gene therapy, due to the potential for persistent biological activity of the genetic material or other product components used to carry the genetic material. **Accordingly, the FDA typically recommends an extended follow- up period to monitor for such events in patients who have received investigational gene therapies. Although we have communicated to the FDA our intent to withdraw or inactive our previously open INDs and discontinue development of our product candidates, as well as our determination that such long- term follow- up is not necessary for our product candidates, the FDA may disagree, and may continue to recommend that such follow- up be conducted.** If **we resume development of our product candidates and** unacceptable side effects arise in the development of ~~our~~ **such** product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted or DMC, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment- related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly. If **we resume development of our product candidates and** any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long- term follow- up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including: • regulatory authorities may withdraw approvals of such product; • we may be required to recall a product or change the way such product is administered to patients; • additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product; • regulatory authorities may require additional warnings on the label, such as a " black box " warning or contraindication; • we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients or implement similar risk management measures; • the product could become less competitive; • we could be sued and held liable for harm caused to patients; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects. The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable ~~, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed~~ . The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but 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, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and ~~it~~ **have communicated to the FDA our intent to withdraw or inactivate our previously open INDs. It** is possible that neither our ~~current~~ product candidates **previously in development (should we elect to restart our development programs)** , nor any other product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of a BLA from the FDA. It is possible that the FDA may refuse to file for substantive review any BLAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. Similar risks exist in foreign jurisdictions. Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well- controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory authorities, that such product candidates are safe and effective, or in the case of biologics, safe, pure, and potent, for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical 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 and other regulatory authorities may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post- approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other FDA- and other regulatory authorities- required studies, approval of any BLA or application that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available. Of the large number of potential products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post- marketing clinical trials, including Phase 4 clinical trials, and / or the implementation of a REMS or similar risk management measures, which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates. In

addition, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the EC in November 2020. The EC' s proposal for revision of several legislative instruments related to medicinal products (**including** potentially revising the duration of regulatory exclusivity ~~,~~ **and** eligibility for expedited pathways ~~, etc.~~) **was published on April 26,** ~~is currently expected to be adopted enduring the first quarter of~~ 2023. The proposed revisions **remain to be** ~~, once they are~~ agreed and adopted by the European Parliament and European Council (not expected before the end of 2024 or early 2025) **. The revisions** may **, however,** have a significant impact on the pharmaceutical industry **and our business** in the long term. Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business **to the extent we resume such activities** . The ability of the FDA and foreign regulatory authorities to review and or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s or and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s or foreign regulatory authorities' ability to perform routine functions. Average review times at the agency and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA following its relocation to Amsterdam and related reorganization, may also slow the time necessary for new drugs and biologics to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. ~~Also, resource constraints resulting from the COVID- 19 pandemic have caused and could continue to cause the FDA and / or other agencies to be unable to provide requested feedback to companies navigating the regulatory review process on a timely basis. Separately, in response to the COVID- 19 pandemic, in March 2020, the FDA postponed most inspections of domestic and foreign manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on- site inspections of domestic manufacturing facilities subject to a risk- based prioritization system. The FDA utilized this risk- based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, in April 2021, the FDA began conducting voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites in circumstances where the FDA determines that such remote evaluation would be appropriate based on mission needs and travel limitations. In July 2021, the FDA resumed standard inspectional operations of domestic facilities. Since that time, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID- 19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.~~ Even if we **restart development of our product candidates and** obtain FDA approval for our product candidates in the United States **in the future** , we may never obtain approval for or commercialize 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 does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in **any** 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. Even if we **restart development of and** receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates. Any product candidate for which we obtain marketing approval, ~~along with~~ **will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities, including oversight of** the manufacturing processes, post- approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, among other things ~~, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities~~ . These requirements include submissions of safety and other post- marketing information and reports, establishment registration and drug listing requirements, continued compliance with GMP requirements relating to manufacturing, quality control, quality

assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post- approval. Manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with ~~cGMP~~ **GMP** or similar regulations and standards. In addition, any marketing approvals that we may receive for our product candidates may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post- approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including: • restrictions on manufacturing such products; • restrictions on the labeling or marketing of a product; • restrictions on product distribution or use; • requirements to conduct post- marketing studies or clinical trials; • warning letters or holds on clinical trials; • withdrawal of the products from the market; • refusal to approve pending applications or supplements to approved applications that we submit; • recall of products; • fines, restitution or disgorgement of profits or revenues; • suspension or withdrawal of marketing approvals; • refusal to permit the import or export of our products; • product seizure or detention; or • injunctions or the imposition of civil or criminal penalties. The FDA' s and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability. The FDA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off- label uses. If **we restart development of our product candidates and** any of our product candidates are approved **,** and we are found to have improperly promoted off- label uses of those products, we may become subject to significant liability. The FDA and other regulatory authorities strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product' s approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off- label uses, we may become subject to significant liability. The U. S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off- label use and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition. Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop. The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in: • impairment of our business reputation and significant negative media attention; • withdrawal of participants from our clinical trials; • significant costs to defend the related litigation and related litigation; • distraction of management' s attention from our primary business; • substantial monetary awards to patients or other claimants; • inability to commercialize our product candidates; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • decreased demand for our product candidates, if approved for commercial sale; and • loss of revenue. Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities. We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, umbrella, and directors' and officers' insurance. Any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any of our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. We also expect that operating as a public company will continue to make it more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher

costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations. Our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization **, to the extent we resume such activities,** may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business. Misconduct by our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, foreign regulatory authorities rules and regulations and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations ~~; or (iv) laws that require the reporting of true, complete and accurate financial information and data~~ . Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U. S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations. Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity. In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Our information technology systems, as well as those of our CROs and other contractors and consultants, are vulnerable to failure or damage from computer viruses and malware (e. g. ransomware), unauthorized access or other cybersecurity attacks, natural disasters (including hurricanes), **international** terrorism, **conflicts** ~~war (including the war between Russia and Ukraine)~~ and telecommunication and electrical failures. ~~If~~ **We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if** such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs. For example **, should we resume the development of our product candidates** , the loss of preclinical or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to human error (e. g., social engineering, phishing), a technical vulnerability, malfeasance or other disruptions. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. **We** ~~As a result of the COVID- 19 pandemic, we~~ may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques **(including artificial intelligence)** that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. Any significant security breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could **require significant resources to remediate or recover from the incident,** result in legal claims or proceedings **(including class actions)** , liability under laws that protect the privacy of personal information, significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates. Further, our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. **Should we resume development of our product candidates,** ~~Initial~~ **initial** , interim, " top- line " and preliminary data 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. **If** ~~From time to time,~~ we

resume development of our product candidates, we may publicly disclose initial, interim, top- line or preliminary data from our clinical trials, which ~~is~~ **would be** based on a preliminary analysis of then- available data, and the results and related findings and conclusions ~~are~~ **would be** subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the initial, top- line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Initial, top- line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the initial, top- line or preliminary data we previously published. **Should we resume development of our product candidates, further clinical data from any trials of our candidates may not be consistent with data previously observed and disclosed in preclinical studies or clinical trials.** As a result, initial, top- line and preliminary data should be viewed with caution until the final data are available. **We may** ~~From time to time, we~~ also disclose interim or initial data from our preclinical studies and clinical trials. Interim or initial data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between initial, interim, top- line or preliminary data and final data could significantly harm our business prospects. Further, disclosure of any such data by us or by our competitors could result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our Company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the top- line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. ~~We~~ **To the extent we resume development of our product candidates, 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 managerial resources, we **have** ~~focus~~ **focused** on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable 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. Risks Related to Healthcare Laws and Other Legal Compliance Matters **If we resume development of our product candidates,** ~~Enacted~~ **enacted** and future healthcare legislation ~~may~~ **could** increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set. In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in ~~March~~ 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following: • an annual, non- deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs; • a ~~new~~ Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 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; • an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23. 1 % and 13. 0 % of the average manufacturer price for branded and generic drugs, respectively; • ~~a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; •~~ extension of a manufacturer' s Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; • expansion of eligibility criteria for Medicaid ~~programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 % of the federal poverty level~~, thereby potentially increasing a manufacturer' s Medicaid rebate liability; **and** • a ~~new~~ Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research ~~; and • establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial, executive, and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA~~. In addition, other legislative changes have been proposed and adopted in the United States since

the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through ~~2032~~ **2031** , unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other healthcare funding, which could negatively affect our customers and accordingly, our financial operations. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory cap on the Medicaid drug rebate, currently set at 100 % of a drug' s AMP, beginning January 1, 2024. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. ~~For~~ **Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for** that ~~and other reasons~~ **disease or condition. If a product receives multiple orphan designations or has multiple approved indications** , it **may not qualify for the orphan drug exemption. The implementation of the IRA** is currently ~~unclear how~~ **the subject of ongoing litigation challenging the constitutionality of** the IRA ~~will be effectuated, and the~~ **' s Medicare drug price negotiation program. The** impact of the IRA on our business and the pharmaceutical industry cannot yet be fully determined **, but it could have a significant impact** . In particular, if a product becomes subject to the IRA negotiation provision and related price cap, that may significantly alter the economic rationale for developing and commercializing a biosimilar. We expect that additional U. S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U. S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally- mandated price controls on payment amounts by third- party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing. In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. On December 13, 2021, Regulation No 2021 / 2282 on Health Technology Assessment, or HTA amending Directive 2011 / 24 / EU, was adopted. While the ~~Regulation~~ **regulation** entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation- related steps to take place in the interim. Once the ~~Regulation~~ **regulation** becomes applicable, it will have a phased implementation depending on the concerned products. ~~This~~ **The** regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation ~~foresees a three- year transitional period and~~ will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to

maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U. S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the U. S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U. S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U. S. federal government. **The federal False Claims Act also permits a private individual acting as a " whistleblower " to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery.** In addition, the government may assert that a claim including items and services resulting from a violation of the U. S. federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act; • The Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U. S. federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices; • the U. S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product; • the U. S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children' s Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; • analogous U. S. state laws and regulations, including: state anti- kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third- party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U. S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals; and • similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers. For instance, in the EU, interactions between pharmaceutical companies and healthcare professionals and healthcare organizations, are also governed by strict laws, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct both at EU level and member states level. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of pharmaceutical products is prohibited in the EU. Relationships with healthcare professionals and associations are subject to stringent anti- gift statutes and anti- bribery laws, the scope of which differs across the EU. In addition, national " Sunshine Acts " may require pharmaceutical companies to report / publish transfers of value provided to healthcare professionals and associations on a regular (e. g. annual) basis. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government- funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which

could affect our ability to operate our business. Further, defending against any such actions can be costly, time- consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. In the United States, HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, or collectively, HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, California enacted the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, increases data privacy obligations for covered companies and provides individual privacy rights to California consumers, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing the likelihood of and risks associated with a data breach. Although the law includes limited exceptions, including for " protected health information " maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. Further, the California Privacy Rights Act, or CPRA, generally went into effect on January 1, 2023 and significantly amends the CCPA. It imposes additional data protection obligations on covered companies doing business in California, including additional consumer rights processes and opt outs for certain uses of sensitive data. It also creates a new California data protection agency specifically tasked to enforce the law, which will likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. The substantive requirements for businesses subject to the CPRA become enforceable on July 1, 2023. Similar laws have passed in ~~Virginia, Colorado, Connecticut and Utah, and have been proposed in~~ other states and **are continuing to be proposed** at the **state and** federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. Furthermore, the Federal Trade Commission, or FTC, and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security practices that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5 (a) of the Federal Trade Commission Act. The FTC expects a company' s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, in Europe, the GDPR imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Economic Area, or EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States **. Case law from** ~~; in July 2020,~~ the Court of Justice of the ~~EU~~ **European Union** , or CJEU, ~~limited how organizations could lawfully transfer personal data from the EU / EEA to the United States~~ **states that reliance** ~~by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions~~ on the ~~use of~~ standard contractual clauses ~~, or SCCs. In March 2022,~~ ~~–~~ **a standard form of contract approved by** the ~~US~~ **European Commission as** ~~and~~ **an** ~~EU announced~~ **adequate personal data transfer mechanism – alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on** a **case** ~~new regulatory regime intended to replace the invalidated regulations; however, this new EU~~ ~~US Data Privacy Framework has not been implemented beyond an executive order signed~~ by ~~President Biden on October 7~~ **- case basis. Following a period of legal complexity and uncertainty regarding international personal data transfers** , **particularly to the** ~~2022 on Enhancing Safeguards for~~ United States **, We expect the** ~~Signals Intelligence Activities. European court and~~ regulatory ~~decisions subsequent~~ **guidance and enforcement landscape** to **continue to develop** ~~the CJEU decision of July 16~~ , ~~2020~~ **in relation to transfers to the United States and elsewhere. As a result, we may** have ~~taken a restrictive approach~~ to **make certain** ~~international~~ **operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing** data transfers **within required time frames** ~~. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results~~ . Since the beginning of 2021, we have also been subject to the UK data protection regime, which imposes separate but similar obligations to those under the GDPR and comparable penalties, including fines of up to £ 17. 5 million or 4 % of a noncompliant company' s global annual revenue for the preceding financial year, whichever is greater. ~~As~~ **If** we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are

evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations. We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities. Our operations ~~, including our development, testing and manufacturing activities,~~ are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood- borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions. As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third- party manufacturers or our development efforts may be interrupted or delayed. We are currently subject to securities class action litigation and may be subject to similar or other litigation in the future, which will require significant management time and attention, result in significant legal expenses and may result in unfavorable outcomes, which may have a material adverse effect on our business, operating results and financial condition, and negatively affect the price of our common stock. We are, and may in the future become, subject to various legal proceedings and claims that arise in or outside the ordinary course of business. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. For example, on March 25, 2022, a stockholder of the Company, Michael C. Pizzuto, filed a putative class action complaint alleging violations of Sections 10 (b) and 20 (a) of the Securities and Exchange Act of 1934, as amended, against us and certain of our executives. Pizzuto v. Homology Medicines, Inc., No. 2: 22 – CV – 01968 (C. D. Cal 2022). The complaint alleges that we failed to disclose certain information regarding efficacy and safety in connection with a Phase 1 / 2 HMI- 102 clinical trial, and seeks damages in an unspecified amount. The Company filed a motion to transfer the case to the United States District Court for the District of Massachusetts on September 2, 2022, and a motion to dismiss on October 17, 2022. **On April 18, 2023,** ~~Both motions are fully briefed and awaiting~~ the court **granted the motion to transfer, finding that venue was not proper in the Central District of California and transferring the case to the District of Massachusetts. Following the transfer, the case number changed to 1: 23- cv- 10858- AK (D. Mass.). On May 9, 2023, the Massachusetts court issued an order permitting the parties to submit updated briefs in connection with the motion to dismiss, which were submitted on June 8, 2023, July 13, 2023, and August 3, 2023. The motion to dismiss remains pending. On March 4, 2024, the Massachusetts court held oral argument on the Company** ' s ~~determination~~ **motion to dismiss, which remains pending. On February 22, 2024, a purported stockholder of the Company, Kevin Welsh, filed a putative class action complaint against the Company and its directors related to the Company' s proposed Merger with Q32, alleging violations of Sections 14 (a) and 20 (a) of the Securities Exchange Act of 1934, as amended. Welsh v. Homology Medicines, Inc., No. 1: 24- cv- 00242 (D. Del.). The complaint alleges that the Company and its directors filed a proxy statement containing material omissions regarding financial forecasts and their respective analysis, and seeks damages in an unspecified amount. The case is in its early stages. The Company believes the claims alleged lack merit** . The results of the securities class action lawsuit and any future legal proceedings cannot be predicted with certainty. Also, our insurance coverage may be insufficient **, and any amounts not covered by insurance will be borne by the combined company. Furthermore** , our assets may be insufficient to cover any amounts that exceed our insurance coverage, and we may have to pay damage awards or otherwise may enter into settlement arrangements in connection with such claims. Any such payments or settlement arrangements in current or future litigation could have a material adverse effect on our business, operating results or financial condition. Even if the plaintiffs' claims are not successful, current or future litigation could result in substantial costs and significantly and adversely impact our reputation and divert management' s attention and resources, which could have a material adverse effect on our business, operating results and financial condition, and negatively affect the price of our common stock. In addition, such lawsuits may make it more difficult to finance our operations. ~~We~~ **Should we resume development of our product candidates, we** face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop. The development and commercialization of new genetic medicine products is highly competitive. Moreover, the gene editing field is characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. ~~We~~ **Should we resume development of our product candidates, we** will face competition with respect to any product candidates that we may seek to develop or commercialize ~~in the future~~ from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs, including PKU, MLD, Hunter syndrome, hemoglobinopathies and ophthalmological diseases. Some of these competitive

products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches. ~~Our~~ **Historically, our** platform and product focus ~~is~~ **has been** the development of genetic medicines using our proprietary AAVHSCs in vivo through a nuclease- free gene editing modality, gene therapy, or GTx- mAb, which is designed to produce antibodies throughout the body. ~~If our current~~ **Should we resume development of such** programs ~~are~~ **, and if our former programs were to be** approved for the indications for which we ~~are currently planning~~ **had been conducting** clinical trials, they may compete with other products ~~currently~~ under development, including gene editing and gene therapy products or other types of therapies, such as small molecule, antibody or protein therapies. If our PKU treatments are approved, they may compete with therapies from American Gene Technologies, BioMarin, Censa Pharmaceuticals, Generation Bio, Nestlé Health Science, Sangamo Therapeutics and Synlogic. However, we believe that only gene therapy or gene editing approaches have the potential to restore the normal Phe biochemical pathway with a single administration. If our Hunter syndrome treatment is approved, it may compete with therapies from Shire and / or GC Pharma. If our MLD treatment is approved, it may compete with therapies from Orchard Therapeutics, Passage Bio and / or Shire. In vivo gene therapy approaches provide potential advantages over ex vivo approaches. There are a number of companies developing nuclease- based gene editing technologies using CRISPR / Cas9, TALENs, meganucleases, Mega- TALs and ZFNs, including but not limited to Beam Therapeutics, bluebird bio, Caribou Biosciences, Cellectis, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Precision BioSciences, Prime Therapeutics and Sangamo Therapeutics and non- nuclease- based technology, including LogicBio Therapeutics **, a wholly- owned subsidiary of Alexion** . Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do **. We have requested withdrawal or inactivation of our previously open INDs, so we are currently not progressing any product candidates through the development process** . Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial ~~opportunity~~ **opportunities** could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non- competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomic or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors. In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and / or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. ~~The~~ **Should we resume development of our product candidates, the** successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third- party payors are essential for most patients to be able to afford prescription medications such as our product candidates, assuming FDA or foreign authorities approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Assuming we obtain coverage for our product candidates by a third- party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Moreover, for drugs and biologics 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 products. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. **Coverage and reimbursement by a third- party payor may depend upon a number of factors, including the third- party payor' s determination that use of a product is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; • cost- effective; and • neither experimental nor investigational.** Third- party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third- party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third- party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third- party therapeutics may limit the amount we will be able to charge for our product candidates. These **third- party** payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. 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. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may

impact physician utilization. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates. There is significant uncertainty related to the insurance coverage and reimbursement of newly- approved products. In the United States, third- party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third- party payors may require pre- approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third- party payors will decide with respect to the coverage and reimbursement for our product candidates. No uniform policy for coverage and reimbursement for products exists among third- party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly ~~from~~ **among third- party** ~~payor~~ **payors** ~~to payor~~ . As a result, the coverage determination process is often a time- consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each **third- party** payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost- containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially- reasonable revenue and profits. Even if a pharmaceutical product obtains a marketing authorization in the EU, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. Governments influence the price of medicinal products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume- based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost- effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low- priced markets exert a commercial pressure on pricing within a country. Moreover, increasing efforts by governmental and 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. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. ~~The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.~~ Even if any of our product candidates receives marketing approval **in the future** , it may fail to achieve market acceptance by physicians, patients, third- party payors or others in the medical community necessary for commercial success. If any of our product candidates receives marketing approval **in the future** , it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. If it does not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to: • the safety, efficacy and potential advantages compared to alternative treatments; • effectiveness of sales and marketing efforts; • the cost of treatment in relation to alternative treatments, including any similar generic treatments; • our ability to offer our products for sale at competitive prices; • the convenience and ease of administration compared to alternative treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the strength of marketing and distribution support; • the timing of market introduction of competitive products; • the availability of third- party coverage and adequate reimbursement; • product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product' s approved labeling; • the prevalence and severity of any side effects; and • any restrictions on the use of our product together with other medications. Because we expect sales of our product candidates, if approved, to generate substantially all of our product revenues for a substantial period, the failure of this product to find market acceptance would harm our business and could require us to seek additional financing. ~~If~~ **Should we resume development of our product candidates, if** we are unable to establish sales, marketing and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates, if approved. Moreover, provisions in our agreements with Pfizer may inhibit our ability to enter into future

collaborations with third parties. We do not have any infrastructure for the sales, marketing or distribution of our products, and the cost of establishing and maintaining such an organization may exceed the cost- effectiveness of doing so. **Should we resume development of** ~~We expect to build a focused sales, distribution and marketing infrastructure to market~~ our product candidates ~~in the United States and EU~~, ~~if approved. There~~ **there** are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact the commercialization of our product candidates. Additionally, if the commercial launch of any of our product candidates 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. We do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of our product candidates in certain markets overseas. Therefore, our future sales in these markets will largely depend on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator' s strategic interest in the product and such collaborator' s ability to successfully market and sell the product. We intend to pursue collaborative arrangements regarding the sale and marketing of our product candidates, if approved, for certain markets overseas; however, we cannot assure that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces. If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of our product candidates, we may be forced to delay the potential commercialization of our product candidates or reduce the scope of our sales or marketing activities for our product candidates. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborative partners at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to our product candidates or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects. ~~Moreover, we have granted Pfizer a right of first refusal to acquire rights (whether through license, asset sale or otherwise) to develop or commercialize HMI- 102 and / or HMI- 103. This right of first refusal provision may inhibit our ability to enter into future collaborations with third parties.~~ If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates, and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well- funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies. If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business. If any of our product candidates are approved for commercialization, we intend to enter into agreements with third parties to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including: • different regulatory requirements for drug and biologic approvals and rules governing drug and biologic commercialization and country- specific regulations of gene therapies in foreign countries; • complex and restrictive import / export regulations; • reduced protection for intellectual property rights; • foreign reimbursement, pricing and insurance regimes; • potential noncompliance with the U. S. Foreign Corrupt Practices Act, the U. K. Bribery Act 2010 and similar anti- bribery and anticorruption laws in other jurisdictions; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; • political and economic instability, including in light of **international terrorism** ~~the war between Russian~~ and ~~Ukraine~~ **conflicts**; • fluctuations in currency exchange rates; and • higher costs of doing business internationally, including increased accounting, travel infrastructure and legal compliance costs. We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the EU and many of the EU member states with which we will need to comply. Many U. S.- based biotechnology companies have found the process of marketing their own products in Europe to be very challenging. ~~Any~~ **In the future, any** product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated. The Patient Protection and Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which 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. 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. Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. 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. We ~~currently~~ **have historically** ~~contract~~ **contracted** with third parties, including Oxford Biomedica ~~Solutions~~ **(US)** LLC, for the manufacture of certain materials for our research programs, preclinical and clinical studies. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost or in compliance with regulatory requirements, which could delay, prevent, or impair our development or commercialization efforts **if we were to resume such activities** . We ~~currently rely~~ **have historically relied** on third- party manufacturers for the manufacture of materials for research programs, preclinical and clinical studies. We do not have long- term supply agreements with all of the third- party manufacturers, and we purchase our required supply on a purchase order basis. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single- source supplier. ~~If~~ **Should we resume development of our product candidates, if** we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. We may be unable to establish any agreements with third- party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: • the possible breach of the manufacturing agreement by the third party; • the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; • reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; • inability to meet our drug specifications and quality requirements consistently; • delay or inability to procure ~~or expand~~ sufficient manufacturing capacity; • issues related to scale- up of manufacturing; • costs and validation of new equipment and facilities required for scale- up; • reliance on single sources for drug components; • lack of qualified backup suppliers for those components that are currently purchased from a sole or single- source supplier; • misappropriation of proprietary information, including our trade secrets and know- how; • the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or study drug or placebo not being properly identified; • clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; • operations of our third- party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and • carrier disruptions or increased costs that are beyond our control. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with ~~cGMP~~ - **GMP** regulations for manufacturing both active drug substances and finished drug products. Third- party manufacturers may not be able to comply with GMP regulations or similar regulatory requirements outside the United States. The failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects. **Assuming we were** ~~It is possible that the COVID- 19 pandemic and response efforts may have an impact in the future on our third- party suppliers and CMOs' ability~~ to ~~manufacture~~ **resume the development of** our product candidates **, any** ~~or materials needed for our preclinical studies and clinical trials. Any~~ medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under GMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis. ~~We intend to continue to~~ **Should we resume development of our product candidates, we would** rely on third parties to conduct, supervise and monitor our clinical trials. If those third parties ~~do~~ **did** not successfully carry out their contractual duties, or if they ~~perform~~ **performed** in an unsatisfactory manner, it may harm our business. ~~We intend to continue to~~ **Should we resume development of our product candidates, we would** rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we expect to have limited influence over their actual performance. We **would** ~~intend to continue to~~ rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future nonclinical studies. Our reliance on CROs for clinical development activities limits our control over these activities, but we ~~will~~ **would** remain responsible for ensuring that each of our studies ~~is~~ **was** conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs ~~does~~ **would** not relieve us of our regulatory responsibilities. We and our CROs will be required to comply with GLP and GCP, which are regulations and guidelines enforced by the FDA and are also required by the competent authorities in the EU and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. The Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA 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 comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under GMP regulations. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process. Our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and nonclinical

programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other product development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations or fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any 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 any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed. If our relationship with any CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional 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 an adverse impact on our business, financial condition and prospects. ~~We~~ **Should we resume development of our product candidates, we** may collaborate with third parties for the development and commercialization of our product candidates **in the future** , but there are no assurances that we will succeed in establishing and maintaining such collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all. ~~We~~ **Should we resume development of our product candidates, we** may seek collaborative relationships for the development and commercialization of our product candidates **in the future** . Failure to obtain a collaborative relationship for any of our product candidates may significantly impair the potential for the product candidate. We **would** also ~~will~~ need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time- consuming and involves significant uncertainty, such as: • a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing; • a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons; • a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration; • a collaboration partner may not devote sufficient capital or resources towards our product candidates; • a collaboration partner may change the success criteria for a product candidate thereby delaying or ceasing development of such candidate; • a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities; • a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate; • a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product; • a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements; • a collaboration partner may terminate a strategic alliance; • a dispute may arise between us and a partner concerning the research, development or commercialization of a product candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and • a partner may use our products or technology in such a way as to invite litigation from a third party. If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital. Moreover, any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us ~~. We do not have multiple sources of supply for all of the components used in our product candidates. If we were to lose a supplier, it could have a material adverse effect on our ability to complete the development of our product candidates, and if we obtain regulatory approval for any of our product candidates, we will need to expand the supply of components prior to commercialization. We do not have multiple sources of supply for all of the components used in the manufacturing of our product candidates. We also do not have long- term supply agreements with any of our component suppliers. It is our expectation that we will only qualify one initial supplier that will need to be approved by the FDA. If for any reason we are unable to obtain product from the manufacturer we select, we would have to qualify new manufacturers. We may not be able to establish additional sources of supply for our product candidates, or may be unable to do so on acceptable terms. Furthermore, pursuant to the terms of the Supply Agreement with OXB Solutions entered into in March 2022, we have agreed to purchase from OXB Solutions at least 50 % of our clinical supply requirements of AAV- based products during the initial term of the Supply Agreement. If we were to experience an unexpected loss of supply from OXB Solutions for any reason, this could result in a delay in our desired clinical and commercial timelines. Manufacturing suppliers are subject to GMP quality and regulatory requirements, covering manufacturing, testing, quality control and record keeping relating to our product candidates and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions in supply. Manufacturing suppliers are also subject to local, state and federal regulations and licensing requirements. Failure by any of our suppliers to comply with all applicable regulations and requirements may result in long delays and interruptions in supply. The number of suppliers of the~~

~~raw material components of our product candidates is limited. In the event it is necessary or desirable to acquire supplies from alternative suppliers, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company. As part of any marketing approval, a manufacturer is required to be licensed by the FDA or foreign regulatory authorities prior to commercialization. This licensing process normally includes inspections by regulatory authorities that must be successful prior to them being licensed. Failure of manufacturing suppliers to successfully complete these regulatory inspections will result in delays. If supply from the approved supplier is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through a BLA amendment or supplement and / or marketing authorization application amendment or supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. If we are unable to obtain the supplies we need at a reasonable price or on a timely basis, it could have a material adverse effect on our ability to complete the development of our product candidates or, if we obtain regulatory approval for our product candidates, to commercialize them~~ . If we fail to comply with our obligations in the agreements under which we in- license or acquire development or commercialization rights to products, technology or data from third parties, we could lose such rights that are important to our business. We are a party to agreements with ~~Caltech~~ **COH** for certain AAV vector- related patents ~~owned by Caltech for human therapeutic applications, or the Caltech License, and COH for certain AAV vector- related patents~~ and know- how, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us. ~~For example, in exchange for the rights granted to us under the Caltech License, we are obligated to pay Caltech up to a total of $ 7. 2 million in milestone payments for the first licensed product, royalties, in the low single- digit percentages, on net sales of licensed products subject to a certain annual minimum royalty, and mid single- to high single- digit percentages of sublicensing revenues.~~ If we fail to comply with our obligations under the ~~Caltech~~ **COH** License, or any of our other collaborators, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements 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. Risks Related to Our Intellectual Property If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets. We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to all current and future product candidates. We seek to protect our proprietary position by filing or collaborating with our licensors to file patent applications in the United States and abroad related to our proprietary technologies, development programs and product candidates. The patent prosecution process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own or in- license may fail to result in issued patents with claims that cover our proprietary products and technology, including our product candidates in the United States or in other foreign countries, in whole or in part. Alternately, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or later invalidate or narrow the scope of an issued patent. Even if patents do successfully issue and even if such patents cover our ~~current~~ **former** product candidates or any future product candidate, third parties may challenge their validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful challenge to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates or companion diagnostic that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate and companion diagnostic under patent protection could be reduced. If the patent applications we hold or have in- licensed with respect to our development programs and product candidates fail to issue, if their validity, breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our ~~current~~ **former** product candidates or any future product candidate, it could dissuade companies from collaborating with us to develop product candidates, encourage competitors to develop competing products or technologies and threaten our ability to commercialize future product candidates. Any such outcome could have a materially adverse effect on our business. The patent position of biotechnology and pharmaceutical companies is highly uncertain, involves complex legal and factual questions, and is characterized by the existence of large numbers of patents and frequent litigation based on allegations of patent or other intellectual property infringement or violation. In addition, the laws of jurisdictions outside the United States may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Since patent applications in the United States and other jurisdictions are confidential for a period of time after filing, we cannot be certain that we were the first to file for patents covering our inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly

uncertain. Our pending and future patent applications may not result in the issuance of patents, or may result in the issuance of patents which fail to protect our technology or products, in whole or in part, or which fail to effectively prevent others from commercializing competitive technologies and products. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Thus, even if our patent applications issue as patents, they may not issue in a form that will provide us with meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of our product candidates, prohibit our use of proprietary technology or sale of products or put our patents and other proprietary rights at risk. Our commercial success depends, in part, upon our ability to develop, manufacture, market and sell our product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical and biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the U. S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous United States, EU and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates, and as the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. We may be subject to third- party claims including infringement, interference or derivation proceedings, post- grant review and inter partes review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if such claims are without merit, a court of competent jurisdiction could hold that these third- party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to prohibit our use of those compositions, formulations, methods of treatment, prevention or use or other technologies, effectively blocking our ability to develop and commercialize the applicable product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we obtained a license. In addition, defending such claims would cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party' s patent rights. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. Further, if a patent infringement suit is brought against us or our third- party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross- license under our intellectual property rights. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might also be forced to redesign or modify our product candidates so that we no longer infringe the third- party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. In addition, if the breadth or strength of protection provided the patents and patent applications we own or in- license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty,

obviousness or non- enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information, or made a misleading statement. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, 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, and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace. We may not identify relevant third- party patents or may incorrectly interpret the relevance, scope or expiration of a third- party patent which might adversely affect our ability to develop, manufacture and market our product candidates. We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third- party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, EU and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could be filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent' s prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third- party patent or may incorrectly predict whether a third party' s pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States, the EU or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates. If we fail to correctly identify or interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay monetary damages, we may be temporarily or permanently prohibited from commercializing our product candidates. We might, if possible, also be forced to redesign our product candidates in a manner that no longer infringes third- party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and genetic medicines industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biotechnology and genetic medicines patents is costly, time- consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U. S. patent system. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a " first- to- invent " to a " first- to- file " system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a " first- to- file " system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application and diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U. S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings as compared to the evidentiary standard in U. S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even

though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents. We may become involved in opposition, interference, derivation, inter partes review or other proceedings challenging our or our licensors' patent rights, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our owned or in- licensed patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. Additionally, the U. S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but, the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. The USPTO and European and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and European and other patent agencies over the lifetime of a patent. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non- compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non- compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved. We 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, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In- licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in- licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the EU. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. In addition, we **intend** ~~may decide~~ to abandon **certain** national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail,

damages or other remedies awarded to us, 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. Furthermore, 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 or our licensors 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 in those jurisdictions. In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions. If we do not obtain patent term extension in the United States under the Hatch- Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be materially harmed. The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non- provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review and approval of new product candidates, patents protecting such candidates may expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch- Waxman Act, which permits 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. In the EU, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, 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. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial. Our proprietary rights may not adequately protect our technologies and product candidates, and 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 the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed; • others, including inventors or developers of our owned or in- licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing our intellectual property rights; • we or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license; • we or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license; • we or our licensors may fail to meet obligations to the U. S. government with respect to in- licensed patents and patent applications funded by U. S. government grants, leading to the loss of patent rights; • it is possible that our pending patent applications will not result in issued patents; • it is possible that there are prior public disclosures that could invalidate our or our licensors' patents; • issued patents that we own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • ownership, validity or enforceability of our or our licensors' patents or patent applications may be challenged by third parties; and • the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business. We depend on proprietary technology licensed from others. If we lose our existing licenses or are unable to acquire or license additional proprietary rights from third parties, we may not be able to continue developing our products. We currently in- license certain intellectual property from COH ~~and Caltech~~ . In the future we may in- license intellectual property from other licensors. We rely on certain of these licensors to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We have limited control over these activities or any other intellectual property that may be related to our in- licensed

intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third- party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves. The licensing and acquisition of third- party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third- party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business. We are a party to license agreements with COH ~~and Caltech~~, pursuant to which we in- license patents and technology for our product candidates. These existing licenses impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations or otherwise materially breach a license agreement, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property. In addition, any claims asserted against us by our licensors may be costly and time- consuming, divert the attention of key personnel from business operations or otherwise have a material adverse effect on our business. Our reliance on third parties may require us to share our trade secrets, which increases the possibility that our trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information. We consider proprietary trade secrets, confidential know- how and unpatented know- how to be important to our business. We may rely on trade secrets and confidential know- how to protect our technology, especially where patent protection is believed by us to be of limited value. However, trade secrets and confidential know- how are difficult to protect, and we have limited control over the protection of trade secrets and confidential know- how used by our licensors, collaborators and suppliers. Because we expect to rely on third parties to manufacture our current and future product candidates, and we expect to collaborate with third parties on the development of our current and future product candidates, we may, at times, share trade secrets with them. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development collaborations or similar agreements. Under such circumstances, trade secrets and confidential know- how can be difficult to maintain as confidential. To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with us 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. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. 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 competitive 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 would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets and / or confidential know- how is expensive, time consuming and unpredictable, and the enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. 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, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third- party collaborators. A competitor' s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. As of December 31, ~~2022~~ **2023** we own ~~three~~ **four** registered trademarks and ~~two~~ **one** pending trademark ~~applications~~ **application** in the United States, as well as ~~38~~ **39** registered trademarks and ~~seven~~ **five** pending trademark applications in other countries around the world. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations ~~. We may need to license additional intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms. The~~

~~growth of our business may depend in part on our ability to acquire or in- license additional proprietary rights. For example, our programs may involve product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compositions and pre- existing pharmaceutical compositions. These pharmaceutical products may be covered by intellectual property rights held by others. We may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in- license any relevant third- party intellectual property rights that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third- party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license under such intellectual property rights, any such license may be non- exclusive, which may allow our competitors access to the same technologies licensed to us~~ . We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties. We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to 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 patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and 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. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees. Risks Related to Employee Matters and ~~Managing Growth and~~ Other Risks Related to Our Business ~~The COVID~~

Our recent reduction in force undertaken to significantly reduce our ongoing operating expenses may not result in our intended outcomes and may yield unintended consequences and additional costs. In July 2023, we implemented a reduction in force affecting approximately 80 employees, or 86 % of our workforce, in order to reduce our ongoing operating costs, extend our cash runway and maximize shareholder value as we consider strategic options. In connection with this corporate restructuring, we recorded a restructuring charge for severance and related costs of $ 10. 3 million in the Company' s consolidated statements of operations included elsewhere in this Annual Report on Form 10 - **K during** ~~19 pandemic has and could continue to adversely impact our business, including our preclinical studies and clinical trials. Disruptions caused by~~ the **twelve months ended December 31, 2023** ~~COVID- 19 pandemic have resulted in delays in enrolling our Phase 1 / 2 pheNIX clinical trial~~ . In addition, ~~many clinical sites are under~~ **we had previously granted certain of the terminated employees restricted stock units that vest in annual installments based on continued service to the Company, as well as options to purchase shares of the Company' s common stock that typically vest over a period of four years. In connection with the reduction in workforce, the Company agreed to accelerate the vesting of a portion of the RSUs that were unvested as of the employees' termination dates, and also modify the stock options for terminated employees such that subject to the satisfaction of severance conditions, the terminated employees' vested options will remain outstanding and exercisable until the first anniversary of each employee' s termination date. These equity modifications resulted in a net reduction to stock based compensation expense of $ 1. 0 million reflected within restructuring and other charges in the Company' s consolidated statements of operations included elsewhere in this Annual Report on Form 10** - ~~resourced~~ **K during the twelve months ended December 31, 2023. The reduction in force may result in unintended consequences and additional costs, such** as ~~a result of COVID- 19 and other~~ -- **the loss** ~~factors, impacting the sites' ability to advance clinical trials in a timely manner. We could experience disruptions in conducting or completing our other ongoing and planned preclinical and clinical trials and could incur unforeseen costs as a result~~ of **institutional knowledge** ~~preclinical study or clinical trial delays. While we have entered into arrangements with third parties to provide remote patient visits and monitoring, we may still experience delays with our ongoing and planned clinical trials. It is possible that the COVID- 19 pandemic may have an~~ **and expertise, attrition beyond** ~~impact in the future on our CROs' ability to complete critical studies required for the progression of these~~ -- **the** ~~programs. Moreover~~ **intended number of employees** , **decreased morale among** ~~it is possible that the COVID- 19 pandemic and response efforts may have an impact in the future on our third- party suppliers and CMOs' ability to manufacture our product candidates or~~ **our remaining employees** ~~materials needed for our preclinical studies and clinical trials. If the COVID- 19 pandemic and disruptions caused by government actions to limit its spread continue for a significant length of time~~ , ~~we may experience additional disruptions that could severely impact our business, preclinical studies~~ and ~~clinical trials, including: • delays in receiving approval from local regulatory authorities to initiate our planned clinical trials; • delays or difficulties in enrolling patients in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • delays in clinical sites receiving~~ the ~~supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials; •~~ risk that **we may not achieve** ~~participants enrolled in our clinical trials will acquire COVID- 19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; • interruptions or delays in preclinical studies due to restricted or limited operations at our research and development laboratory facility; • limitations in employee resources that would otherwise be focused on the conduct of our~~

~~clinical trials, including because of sickness of employees or their~~ -- **the anticipated benefits** ~~families or the desire~~ of ~~employees to avoid contact with large groups of people; • refusal of~~ the **reduction** ~~FDA to accept data from clinical trials~~ in **force** ~~affected geographies; and • impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans. As the COVID- 19 pandemic continues to evolve, the extent to which the pandemic may further impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence. While the economic impact brought by and the duration of the COVID- 19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, which could reduce our ability to access capital and negatively affect our liquidity~~ . In addition, ~~the recession~~ **while positions have been eliminated certain functions necessary to** ~~or~~ **our operations remain, and we may be unsuccessful in distributing the duties and obligations of departed employees among our remaining employees. The reduction in workforce could also** ~~market~~ -- **make** ~~correction resulting~~ **it difficult for us to pursue, or prevent us** from **pursuing, new opportunities and initiatives due to insufficient personnel, or require us to incur additional and unanticipated costs to hire new personnel to pursue such opportunities or initiatives. If we are unable to realize** the ~~spread~~ **anticipated benefits from the reduction in force, or if we experience significant adverse consequences from the reduction in force, our business, financial condition, and results** of **operations may be** ~~COVID- 19 could~~ materially **adversely** ~~affect~~ **affected** ~~our business~~ . Our future success depends on our ability to retain our key personnel and to attract, retain and motivate qualified personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of **certain** ~~Albert Seymour, Ph. D., our President and Chief Executive Officer, as well as the other~~ principal members of our management ~~, scientific and clinical~~ teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. ~~If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. 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 develop, gain regulatory approval of and commercialize product candidates successfully. We recently experienced a modest workforce reduction commensurate with our previously disclosed pipeline prioritization. We have also incurred increased expenses in connection with the hiring of new employees, and we expect these increased costs to continue. Competition to hire from the limited pool of skilled workers discussed above is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.~~ We or the third parties upon whom we depend may be adversely affected by natural disasters public health emergencies and other natural catastrophic events, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, public health emergency, such as the COVID- 19 pandemic, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. For example, following Hurricane Maria, shortages in production and delays in a number of medical supplies produced in Puerto Rico resulted, and any similar interruption due to a natural disaster affecting us or any of our third- party manufacturers could materially delay our operations. Risks Related to Our Common Stock Our executive officers and directors and their respective affiliates, if they choose to act together, will continue to have the ability to control or significantly influence all matters submitted to stockholders for approval. Our executive officers and directors and their respective affiliates, in the aggregate, hold shares representing approximately ~~18~~ **10** . ~~5~~ **2** % of our outstanding voting stock as of December 31, ~~2022~~ **2023** . As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation or sale of all or substantially all of our assets. A significant portion of our total outstanding shares are eligible, or will soon become eligible, to be sold into the market, which could cause the market price of our common stock to drop significantly, even if our business is doing well. Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. We have registered all shares of common stock that we may issue under our equity compensation plans, which can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates ~~. We are an " emerging growth company, " and the reduced disclosure requirements applicable to emerging growth companies may make our common stock 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 may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the closing of the initial public offering of our common stock. However, if certain events occur prior to the end of such five- year period, including if we~~

become a " large accelerated filer, " our annual gross revenues exceed $ 1. 235 billion or we issue more than $ 1. 0 billion of non- convertible debt in any three- year period, we will cease to be an emerging growth company prior to the end of such five- year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include: • not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting; • not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements; • reduced disclosure obligations regarding executive compensation; and • exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period . Provisions in our restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of our Company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our Company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing: • a classified board of directors with three- year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors; • no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates; • the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors; • the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer; • the ability of our board of directors to alter our bylaws without obtaining stockholder approval; • the required approval of the holders of at least two- thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors; • a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders; • the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and • advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer' s own slate of directors or otherwise attempting to obtain control of us. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Our certificate of incorporation designates the Court of Chancery of the State of Delaware, subject to certain exceptions, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders and our bylaws designate the federal district courts of the United States as the exclusive forum for actions arising under the Securities Act of 1933, as amended, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation and bylaws described above. We believe these choice of forum provisions benefit us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi- forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees and agents as it may limit any stockholder' s ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees or agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation

or bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provisions contained in our restated certificate of incorporation or bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations. Our ability to use net operating losses and research and development credits to offset future taxable income or income tax liabilities may be subject to certain limitations. As of December 31, ~~2022~~ **2023**, we had federal and state net operating loss carryforwards, or NOLs, of approximately $ ~~283~~ **326** ~~5~~ **2** million and $ ~~272~~ **317** ~~1~~ **3** million, respectively. Our state NOLs, and federal NOLs generated in taxable years beginning before January 1, 2018, are subject to expiration and will expire at various dates through ~~2041~~ **2043**. Federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely but may only be used to offset 80 % of our taxable income in taxable years beginning after December 31, 2020, which may require us to pay federal income taxes in future years despite generating federal NOLs in prior years. As of December 31, ~~2022~~ **2023**, we also had federal and state research and development and other tax credit carryforwards, or credits, including the orphan drug credit, of approximately $ ~~55~~ **65** ~~1~~ **5** million and $ ~~14~~ **17** ~~8~~ **2** million, respectively, available to reduce **or offset** future **taxable** income ~~tax liabilities~~. The federal and state credits expire at various dates through ~~2041~~ **2043**. These NOLs and credits could expire unused and be unavailable to offset future taxable income ~~or income tax liabilities~~, to the extent subject to expiration. In addition, in general, under Sections 382 and 383 of ~~the Internal Revenue Code of 1986, as amended, or~~ the Code, a corporation that undergoes an " ownership change " is subject to limitations on its ability to utilize its pre- change NOLs or credits to offset future taxable income ~~or income tax liabilities~~. For these purposes, an ownership change generally occurs where the aggregate change in stock ownership of one or more stockholders or groups of stockholders owning at least 5 % of a corporation' s stock exceeds 50 percentage points over a rolling three- year period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, if any. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change. Our state NOLs or credits may also be impaired or subject to limitations under state law. Accordingly, even if we attain profitability, we may not be able to utilize a material portion of our NOLs or credits. Because we do not anticipate paying any cash dividends on our common shares in the foreseeable future, capital appreciation, if any, would be your sole source of gain. We have never declared or paid any cash dividends on our common shares. We currently anticipate that we will retain future earnings for the development ~~,~~ **and** operation ~~and expansion~~ of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common shares would be your sole source of gain on an investment in our common shares for the foreseeable future. General Risk Factors The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock. Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares of common stock at or above the price at which you purchased them. The market price for our common stock may be influenced by many factors, including: • the success of competitive products or technologies; • actual or expected changes in our growth rate relative to our competitors; • results of clinical trials of our product candidates or those of our competitors; • developments related to our existing or any future collaborations; • regulatory actions with respect to our product candidates or our competitors' products and product candidates; • regulatory or legal developments in the United States and other countries; • development of new product candidates that may address our markets and make our product candidates less attractive; • changes in physician, hospital or healthcare provider practices that may make our product candidates less useful; • announcements by us, our collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our product candidates or clinical development programs; • failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public; • the results of our efforts to discover, develop, acquire or in- license additional product candidates or products; • actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry and market conditions; and • the other factors described in this " Risk Factors " section. We expect to continue to incur increased costs as a result of operating as a public company, and our management **is** ~~will be~~ required to devote substantial time to new compliance initiatives and corporate governance practices. As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes- Oxley Act of 2002, the Dodd- Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq ~~Global Select Market~~ and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel ~~need to~~ devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time- consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors. We ~~are~~ **continue to** ~~evaluating~~ **evaluate** these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. Pursuant to Section 404 of the Sarbanes- Oxley Act of 2002, or

Section 404, we are required to furnish a report by our management on our internal control over financial reporting ~~. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm~~ . To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could cause us to need to restate our previously issued financial statements and result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. There can be no assurance that we will be able to comply with the continued listing standards of Nasdaq. If we fail to satisfy Nasdaq' s continued listing requirements, Nasdaq may take steps to delist our securities. Such a delisting would likely have a negative effect on the price of the securities and would impair stockholders' ability to sell or purchase the securities when they wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our securities to become listed again, stabilize the market price or improve the liquidity of our securities, or prevent future non- compliance with Nasdaq' s listing requirements. ~~We~~ **In the future, we** may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources. In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day- to- day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results. Unstable global political or economic conditions may have serious adverse consequences on our business, financial condition and share price. The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. If the equity and credit markets continue to deteriorate, or the United States enters a recession, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. In addition, ~~the current military~~ **international terrorism and** ~~conflict~~ **conflicts** ~~between Russia and Ukraine~~ could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U. S., the EU or Russia (e. g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and / or our supply chain, our CROs, CMOs and other third parties with which we conduct business. Any of the foregoing could harm our business, results of operations and the price of our common stock may be adversely affected. We are exposed to fluctuations in inflation, which could negatively affect our business, financial condition and results of operations. The United States has recently experienced historically high levels of inflation. According to the U. S. Department of Labor, the annual inflation rate for the United States was approximately 8. 0 % for 2022. If the inflation rate continues to increase, it will likely affect our expenses, including, but not limited to, increased cost of drug product from OXB ~~Solutions~~ **(US) LLC** and other future potential contract manufacturing organizations, supplies and employee compensation expenses. To the extent inflation results in rising interest rates and has other adverse effects on the market, it may adversely affect our business, financial condition and results of operations. The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results. There has been increasing public focus by investors, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, we may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition. Moreover, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.