Risk Factors Comparison 2024-02-22 to 2023-03-23 Form: 10-K

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You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10- K, including the " Management' s Discussion and Analysis of Financial Condition and Results of Operations " section and our consolidated financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed. This report also contains forward- looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward- looking statements as a result of factors that are described below and elsewhere in this report. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part. Risks Relating to Our Business and the Development of Our ~~Product~~ **Drug** Candidates We are a late clinical- stage biopharmaceutical company with a limited operating history. We are a late clinical- stage biopharmaceutical company focused on developing small molecules **engineered** to restore neuronal health and slow neurodegeneration. Our limited operating history may make it difficult to evaluate the success of our business. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. To date, we have not completed a pivotal clinical trial, obtained marketing approval for any ~~product~~ **drug** candidate, manufactured a commercial scale ~~product~~ **drug** candidate ~~, arranged for a third party to do so on our behalf~~ , or conducted sales and marketing activities necessary for successful ~~product~~ **drug** candidate commercialization. Our history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical- stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to overcome such risks and difficulties successfully. If we do not address these risks and difficulties successfully, our business will suffer. We may fail to or be unable to design and execute clinical trials to support marketing approval of fosgonimeton or any of our other ~~product~~ **drug** candidates. We cannot be certain that our current or planned clinical trials or any other future clinical trials will be completed on time or be successful. We cannot guarantee that the ~~U. S. Food and Drug Administration, or~~ FDA ~~,~~ or foreign regulatory authorities will agree with our study design, protocol or protocol amendments, or statistical plan, or that they will interpret clinical trial results as we do, and more clinical trials could be required before we are able to submit applications seeking approval of our ~~product~~ **drug** candidates. To the extent that the results of the clinical trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional clinical trials in support of potential approval of our ~~product~~ **drug** candidates **(including potential confirmatory or Phase 3 registrational trials)** . Even if regulatory approval is secured for any of our ~~product~~ **drug** candidates, the terms of such approval may limit the scope and use of our ~~product~~ **drug** candidate, which may also limit its commercial potential. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives. Our business depends entirely on the successful discovery, development and commercialization of our ~~product~~ **drug** candidates. We have no **drug** products approved for commercial sale and do not anticipate generating any revenue from **drug** product sales for the next several years, if ever. Our ability to generate **drug** product revenue will depend heavily on the successful clinical development and eventual commercialization of fosgonimeton and one or more of our other future ~~product~~ **drug** candidates. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives, including: • successful and timely completion of nonclinical and clinical development of our ~~product~~ **drug** candidates and any future ~~product~~ **drug** candidates, as well as the associated costs, including any unforeseen costs ; • establishing and maintaining relationships with contract research organizations, or CROs, and clinical sites for the clinical development, both in the United States and internationally, of our ~~product~~ **drug** candidates and any future ~~product~~ **drug** candidates ; • timely **submission of application for and** receipt of marketing approvals from applicable regulatory authorities for any ~~product~~ **drug** candidates for which we successfully complete clinical development ; • making any required post- marketing approval commitments to applicable regulatory authorities ; • developing an efficient and scalable manufacturing process for our ~~product~~ **drug** candidates, including obtaining finished products that are appropriately packaged for sale ; • establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for ~~product~~ **drug** candidates that we develop, if approved ; • successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether inhouse or with one or more collaborators ; • a continued acceptable safety profile following any marketing approval of our ~~product~~ **drug** candidates ; • commercial acceptance of our ~~product~~ **drug** candidates by patients, the medical community and third- party payors ; • identifying, assessing and developing new ~~product~~ **drug** candidates ; • obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally; • protecting our rights in our intellectual property portfolio ; • defending against third- party interference or infringement claims, if any ; • negotiating favorable terms in any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our ~~product~~ **drug** candidates ; • obtaining coverage and adequate reimbursement by hospitals, government and third- party payors for ~~product~~ **drug** candidates that we develop ; • addressing any competing therapies and technological and market developments ; and • attracting, hiring and retaining qualified personnel. We may never be successful in achieving our objectives and, even if we are, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase

profitability on a quarterly or annual basis. Our failure to become and remain profitable may decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our ~~product~~ **drug** candidates on a timely or profitable basis, if at all. Changes in the manufacturing process or facilities will require further comparability analysis and approval by the FDA before implementation, which could delay our clinical trials and ~~product~~ **drug** candidate development, and could require additional clinical trials, including bridging studies **and potential confirmatory or Phase 3 registrational trials** , to demonstrate consistent and continued safety and efficacy. We have not previously submitted **an** ~~a new drug application, or~~ NDA ~~,~~ to the FDA or similar approval filings to a comparable foreign regulatory authority, for any ~~product~~ **drug** candidate. An NDA or other relevant regulatory filing must include extensive nonclinical and clinical data and supporting information to establish that the ~~product~~ **drug** candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the **drug** product. We cannot be certain that our current or future ~~product~~ **drug** candidates will be successful in clinical trials. Further, even if they are successful in clinical trials, our ~~product~~ **drug** candidates or any future ~~product~~ **drug** candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future ~~product~~ **drug** candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a ~~product~~ **drug** candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights, as well as the availability of competitive products, whether there is sufficient third- party reimbursement and adoption by physicians. Our development of fosgonimeton may never lead to a marketable product. We are developing fosgonimeton as a small molecule aimed at restoring neuronal health. We have not received regulatory approval for fosgonimeton and cannot be certain that our approach will lead to the development of an approvable or marketable product, alone or in combination with other therapies. The primary and all secondary endpoints of the ACT- AD **and SHAPE** ~~trial~~ **trials** were not met by protocoled analysis. While we are continuing with the LIFT- AD study, we may not succeed in demonstrating safety and efficacy of fosgonimeton in our LIFT- AD trial or in other clinical trials. Advancing fosgonimeton as a small molecule aimed at restoring neuronal health creates significant challenges for us, including: • obtaining marketing approval; • if fosgonimeton is approved, educating medical personnel regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating fosgonimeton into existing treatment regimens, including in combination with other treatments for AD or as a monotherapy ; and • establishing the sales and marketing capabilities upon obtaining any marketing approvals to gain market acceptance. Our prospects are highly dependent on the successful development of fosgonimeton. If we do not demonstrate the safety and efficacy of fosgonimeton in our LIFT- AD trial, we may explore strategic alternatives to maximize stockholder value, which could involve, without limitation, exploring the potential for a possible merger, business combination, investment, a purchase, license or other acquisition of assets or return of capital to stockholders. Our approach to targeting **neurotrophic** ~~brain growth~~ factors through the use of small molecules is based on a novel therapeutic approach, which exposes us to unforeseen risks. We have limited data from our Phase 1a / 1b and Phase 2 clinical trials to date, and we cannot be certain that future trials will yield data in support of the safety, efficacy and tolerability of our ~~product~~ **drug** candidates. We have discovered and are developing a platform of small molecule ~~product~~ **drug** candidates from which we have selected our lead ~~product~~ **drug** candidate, fosgonimeton, which is under development to treat AD, ~~Parkinson' s Disease Dementia, or~~ PDD, and ~~Dementia with Lewy Bodies, or~~ DLB. Our ~~product~~ **drug** candidates target an endogenous **neurotrophic** ~~brain growth~~ factor which is expected to protect and repair neuronal networks, which we believe could ultimately result in improvements in clinical outcomes and disease- relevant biomarkers. The therapeutic promise of **neurotrophic** ~~brain growth~~ factors in neurodegenerative diseases had been hampered in earlier therapies by the lack of efficient and non- invasive delivery to the ~~brain~~ **CNS** . Our small molecule ~~product~~ **drug** candidates are designed to penetrate the **BBB** ~~blood brain barrier~~ and enhance the activity of a **neurotrophic** ~~brain growth~~ factor, but we cannot be certain of the safety and efficacy of our ~~product~~ **drug** candidates in applicable patients or that our clinical trials will provide sufficient evidence that our design approach results in the intended therapeutic effect. Based on the results of our nonclinical and clinical studies to date, we believe fosgonimeton has the potential to rapidly improve cognition, function and restore the lives of patients suffering from AD. However, these ideas and this approach are novel, and we currently have limited data based on our Phase 1a / b and Phase 2 clinical trials to date. The primary and all secondary endpoints of our Phase 2 ACT- AD clinical trial **in AD** were not met by protocoled analysis. A subsequent post hoc analysis of the data in a pre- specified subgroup from patients on fosgonimeton without background therapy, or AChEIs, showed a meaningful, but not statistically significant, improvement in both ERP P300 latency and cognitive performance compared to placebo at 26 weeks. Although post hoc analyses cannot be used to establish efficacy, these analyses can be helpful in informing the design of current and future clinical studies. Following an unblinded interim efficacy and futility analysis, an independent **DMC** ~~data monitoring committee~~ recommended continuation of the LIFT- AD study of fosgonimeton in patients with mild- to- moderate AD. The committee also determined that, with the additional enrollment of fewer than 150 patients for a total enrollment of less than 300 patients without background therapy (AChEIs), the study will be well powered for the primary endpoint given the preliminary effect size observed. There is no assurance that the amendments to our ongoing LIFT- AD trial based on our findings from the ACT- AD trial and our interim analyses will ultimately result in a successful trial. For example, our biomarker data may not translate into a statistically significant clinical benefit, **the** FDA may not agree with our statistical plan or analyses, or the trial may not be sufficiently powered for our endpoint measures **. In addition, the primary endpoint of our Phase 2 SHAPE clinical trial in PDD and DLB was not met by protocoled analysis. Directionally positive results were observed for the 40 mg fosgonimeton dose group with improvements in cognitive, functional and biomarker measurements. In particular, the five patients in the mITT population treated with fosgonimeton 40 mg once daily saw improvement in ADAS- Cog13 individually, and**

collectively improved compared with placebo (n = 7 mITT, one- sided p = 0. 0321). Results for patients in the 70 mg dose group were inconsistent . Data from our Phase 1a / 1b and Phase 2 clinical trials to date were obtained from a relatively small number of subjects and we cannot be certain that future trials involving a larger number of subjects and clinical sites will yield data in support of the safety, efficacy and tolerability of our ~~product~~ **drug** candidates. We may ultimately discover that fosgonimeton, or any of our other small molecules, do not possess certain properties required for therapeutic effectiveness. We have limited evidence regarding the efficacy, safety and tolerability of fosgonimeton and other small molecules in our **drug** product platform. We may spend substantial funds attempting to develop these ~~product~~ **drug** candidates and never succeed in doing so. We have concentrated our research and development efforts on the treatment of central and peripheral nervous system degenerative disorders, a field that has seen very limited success in product development. We have focused our research and development efforts on addressing ~~central nervous system, or~~ CNS ~~,~~ and ~~peripheral nervous system, or~~ PNS ~~,~~ degenerative disorders. Collectively, efforts by pharmaceutical companies in the field of CNS and peripheral degenerative disorders have seen very limited successes in product development. The development of CNS therapies presents unique challenges, including an imperfect understanding of the biology, the presence of the ~~blood brain barrier, or~~ BBB ~~,~~ that can restrict the flow of drugs to the brain, a frequent lack of translatability of preclinical study results in subsequent clinical trials and dose selection, and the product candidate having an effect that may be too small to be detected using the outcome measures selected in clinical trials or if the outcomes measured do not reach statistical significance. There are few effective therapeutic options available for patients with AD and other CNS or peripheral disorders. Our future success is highly dependent on the successful development of our technology and our ~~product~~ **drug** candidates for treating CNS and peripheral disorders. Developing and, if approved, commercializing our ~~product~~ **drug** candidates for treatment of CNS and peripheral disorders subjects us to a number of challenges, including ensuring that we have selected the optimal doses, executing an appropriate clinical trial to test for efficacy and obtaining regulatory approval from the FDA and other regulatory authorities. An independent special committee of our board of directors engaged in a review of papers co- authored by our former chief executive officer in connection with her doctoral research at **WSU** ~~Washington State University~~ . The special committee' s findings included that (1) our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co- authored while a graduate student at **WSU** ~~Washington State University~~ , and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU' s dihexa patent, exclusively licensed to us, incorporated certain of these altered images. **WSU** ~~Washington State University~~ has undertaken a review of claims of potential research misconduct involving our former chief executive officer' s doctoral research at **WSU** ~~Washington State University~~ . We cannot predict when WSU' s investigation will be completed or what conclusions WSU will reach. An independent special committee of our board of directors engaged in a review of papers co- authored by our former chief executive officer, Dr. Leen Kawas, in connection with her doctoral research at WSU, including, among other things, an investigation of allegations that Dr. Kawas altered images used in research published by Dr. Kawas in connection with her doctoral studies. The independent special committee' s primary finding was that our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co- authored while a graduate student at WSU, and published from 2011 to 2014. While the conduct that was the subject of the allegations is not related to any of our current ~~product~~ **drug** candidates or ongoing clinical research, this finding could have a material adverse effect on our reputation, our in- licensed patents and pending patent applications, licenses and grants, and could lead to further investigation from government agencies, including the FDA, any of which could have a material adverse impact on our business and prospects. As disclosed elsewhere in this report, including in this " Risk Factors " section under the heading " — We and certain of our directors and executive officers have been **, and may in the future be,** named as defendants in lawsuits that could result in substantial costs and divert management' s attention, " and in " Part I, Item 3 — Legal Proceedings, " lawsuits have been filed against us and certain of our directors and officers, alleging violations of federal securities laws related to alleged false and misleading statements in connection with the alleged misconduct of Dr. Kawas and others associated with us. As a result of these allegations and the ongoing litigation against us and certain of our directors and officers and related matters, we have been the subject of negative publicity. This negative publicity may harm our credibility, reputation and relationships with current and future investors, government regulators, patent offices, courts, current and prospective employees, key opinion leaders, prospective collaborators, advocacy groups, current and future patients enrolled in our clinical trials, physicians and prospective patients and vendors. For example, this negative publicity may adversely affect our ability to recruit and hire talented employees, maintain existing business relationships with CROs, clinical trial sites and other parties, enter into new business relationships, enroll patients in our clinical trials, and maintain a viable business in the future. Also, it is possible that the negative publicity and its effect on our work environment could cause our employees to terminate their employment or, if they remain employed by us, result in reduced morale that could have a material adverse effect on our business. In addition, negative publicity has and may continue to adversely affect our stock price and, therefore, employees and prospective employees may be less inclined to seek or continue employment with us. As a result, our business, financial condition, results of operations and cash flows could be materially adversely affected. In addition to the investigation of the independent special committee of our board of directors noted above, WSU has also announced that it has undertaken a review of claims of potential research misconduct involving research conducted by Dr. Kawas during her doctoral studies at WSU. We understand this review is ongoing, and at this time we cannot predict what, if any, effect the investigation will ultimately have on our business and reputation. We are also unable to predict with any certainty when WSU' s investigation will be completed. It is possible that the ongoing investigation by WSU will come to different conclusions, or uncover additional or different information, than the investigation of the independent special committee of our board of directors, the conclusions of which are discussed under " — An independent special committee of our board of directors engaged in a review of papers co- authored by our former chief executive officer in connection with her doctoral research at **WSU** ~~Washington State University~~ . The special committee' s findings included that (1) our former chief executive officer altered images in her 2011

doctoral dissertation and at least four research papers that she co- authored while a graduate student at **WSU** ~~Washington State University~~ , and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU' s dihexa patent, exclusively licensed to us, incorporated certain of these altered images. **WSU** ~~Washington State University~~ has undertaken a review of claims of potential research misconduct involving our former chief executive officer' s doctoral research at **WSU** ~~Washington State University~~ . We cannot predict when WSU' s investigation will be completed or what conclusions WSU will reach ". The conclusions from WSU' s investigation could have a material adverse impact on our business, reputation, scientific credibility, and prospects, as well as our in- licensed patents and pending patent applications, current grants and pending grant applications, and our relationship with WSU, from whom we in- license patents and patent applications underlying certain of our ~~product~~ **drug** candidates. We are and may in the future be subject to claims, lawsuits, arbitration proceedings, government investigations and other legal, regulatory and administrative proceedings and face potential liability and expenses related thereto, which could have a material adverse effect on our business, operating results and financial condition. We are and may in the future be subject to claims, lawsuits, arbitration proceedings, government investigations and other legal, regulatory and administrative proceedings. In November 2022, we received a Civil Investigative Demand from the Civil Division of the Department of Justice, or the Demand. The Demand seeks documents and information relating to our relationship with WSU, certain of our grant applications in 2016 and 2019 with the ~~National Institutes of Health, or~~ NIH, and our receipt of a NIH grant in 2020. We are cooperating with the Department of Justice with respect to the Demand. In February 2023, the Securities and Exchange Commission, or SEC, sent us a subpoena seeking documents and information relating to, among other things, our former chief executive officer' s alteration of images in certain research papers. We are cooperating with the SEC with respect to the subpoena. The outcome of these or any other investigations, claims, or proceedings cannot be predicted with any degree of certainty. In the ordinary course of business we have been and may in the future be the subject of various legal claims. Any such claims, investigations or proceedings against us, whether meritorious or not, could be time- consuming, result in costly litigation, be harmful to our reputation, require significant management attention and divert significant resources, and the resolution of any such claims, investigations or proceedings could result in substantial damages, settlement costs, fines or penalties that could adversely affect our business, financial condition or operating results or result in harm to our reputation and brand, sanctions, consent decrees, injunctions or other remedies requiring a change in our business practices. Further, under certain circumstances we may have contractual or other legal obligations to indemnify and to incur legal expenses on behalf of investors, directors, officers employees, customers, vendors or other third- parties. For example, our amended and restated bylaws provide that we will indemnify our directors and officers, and may indemnify our employees, agents and other persons, to the fullest extent permitted by the Delaware General Corporation Law. We have also entered into indemnification agreements with directors and officers that require us, among other things, to indemnify them against claims that may arise due to their service in those capacities. These indemnification agreements also require us to advance expenses reasonably and actually incurred by them in investigating or defending any such claims, and it may be difficult or impossible to recover any advanced expenses if it turns out the person was not entitled to indemnification. If we are required or agree to defend or indemnify, or advance expenses to, any of our investors, directors, officers, employees, customers, vendors or other third- parties, we could incur material costs and expenses that could adversely affect our business, results of operations or financial condition. Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of early, smaller- scale preclinical studies and clinical trials with a single or few clinical trial sites may not be predictive of eventual safety or ~~effectiveness in large- scale potentially pivotal clinical trials across multiple clinical trial sites.~~ We may encounter substantial delays in clinical trials,or may not be able to conduct or complete clinical trials on the expected timelines,if at all.Our lead ~~drug~~ **product** candidate,fosgonimeton,is in clinical development for the potential treatment of AD,PDD and DLB.Our additional early ~~drug~~ **product** candidates,including ATH- 1105 for ALS,are in preclinical development.It is impossible to predict when or if any of our ~~drug~~ **product** candidates will prove to be effective and safe in humans or will receive regulatory approval.Before obtaining regulatory approvals for the commercial sale of our ~~drug~~ **product** candidates,we must demonstrate through lengthy,complex and expensive nonclinical studies and clinical trials that our ~~drug~~ **product** candidates are both safe and effective for each target indication.Nonclinical and 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 nonclinical study and clinical trial processes,and,because our ~~drug~~ **product** candidates are in an early stage of development,there is a high risk of failure and we may never succeed in developing marketable products.The results of nonclinical studies and early clinical trials of our ~~drug~~ **product** candidates may not be predictive of the results of later- stage clinical trials.Although product candidates may demonstrate promising results in nonclinical studies and early clinical trials,they may not prove to be safe or effective in subsequent clinical trials.For example,testing on animals occurs under different conditions than testing in humans and therefore,the results of animal studies may not accurately predict safety and effectiveness in humans.There is typically an extremely high rate of attrition from the failure of product candidates proceeding through nonclinical studies and clinical trials.Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials.For example,our Phase 1a / b clinical trial,which enrolled 88 patients,including only 11 patients with mild- to- moderate AD,of whom seven patients were treated with fosgonimeton and the other four patients were randomized to the control,suggested improvements in brain network activity including potentially positive effects on brain function.However,our Phase 2 ACT- AD clinical trial ~~in AD~~ ,which included a larger patient population,approximately 60 % of which were receiving standard- of- care AChEIs,did not meet its primary endpoint of a change in ERP P300 latency for the full study population nor did it meet the secondary endpoints.Although a post hoc analysis of results from ACT- AD in a pre- specified subgroup suggested positive effects on measures of cognition,function and neurodegeneration in patients taking fosgonimeton alone without background **acetylcholinesterase inhibitors (** AChEIs **)** ,we cannot be sure that data from future trials will support our earlier findings or demonstrate the safety and effectiveness of

fosgonimeton for treatment of AD to the satisfaction of the FDA ~~and other regulatory authorities~~ in order to support regulatory approval.Likewise,early,smaller- scale studies,biomarker analyses,and clinical trials with a single or relatively few clinical trial sites may not be predictive of **eventual safety and effectiveness in large- scale pivotal clinical trials across multiple clinical trial sites.** effectiveness in large- scale pivotal clinical trials across multiple clinical trial sites. We may encounter substantial delays in clinical..... trials across multiple clinical trial sites. Even if data from a pivotal clinical trial are positive, regulators may not agree that such data are sufficient for approval and may require that we conduct additional clinical trials **(including potential confirmatory or Phase 3 registrational trials)** , which could materially delay our anticipated development timelines, require additional funding for such additional clinical trials, and adversely impact our business. Our ability to achieve regulatory approval for fosgonimeton is further complicated by the nature of AD, which historically has been a challenging indication for drug development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence nonclinical studies and clinical trials are never approved as products. In some instances, there can be significant variability in safety or efficacy results between different nonclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. For example, we believe the topline results of our Phase 2 ACT- AD clinical trial may have differed from the treatment data from our Phase 1a / b clinical trial at least in part due to differences in the patient population and treatment duration, and potential effects from background AChEI treatment. If future trials show that the effect of fosgonimeton when given in combination with add- on standard- of- care AChEIs is diminished, we may be required to seek a narrower indication or restrict our target population to those where fosgonimeton shows a greater effect, which could have a material adverse effect on our business and prospects. On July 6, 2021, we announced the initiation of an open- label extension for the LIFT- AD and ACT- AD trials and in May 2022 we announced the extension of the open label extension for an additional 12 months. ~~Following~~ **In May 2023, we amended the open- label extension trial to further extend the trial by an additional 12 months. Upon** completion of the 26- week treatment period during the LIFT- AD or ACT- AD trials, patients may ~~elect to~~ continue on the open- label extension and receive treatment with fosgonimeton for up to an additional ~~18~~ **30** months. Investigators and patients ~~will~~ remain blinded to treatment group assignment in the original trials. Such open- label extension studies are, and some of the clinical trials we conduct in the future may be, open- label in study design conducted at a limited number of clinical sites on a limited number of patients. An " open- label " clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open- label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open- label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open- label clinical trials are aware when they are receiving treatment. Open- label clinical trials may be subject to a " patient bias " where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open- label clinical trials may be subject to an " investigator bias " where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. We could also encounter delays if a clinical trial is suspended or terminated by us, by the ~~institutional review boards, or~~ IRBs ~~,~~ of the institutions in which such clinical trials are being conducted, by a data safety monitoring board for such clinical trial or by the FDA or comparable foreign regulatory authorities. Clinical trials can be delayed or terminated **or fail to meet endpoints** 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 trials; • the FDA or comparable foreign regulatory authorities disagreeing with our ATH clinical development strategy or statistical plan; • changes in governmental regulations or administrative actions; • delays in our ability to commence a clinical trial; • reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • obtaining IRB approval at each clinical trial site; • recruiting an adequate number of suitable patients to participate in a clinical trial **on a timely basis** ; • the number of patients required for clinical trials of our ~~product~~ **drug** candidates may be larger than we anticipate; • having subjects complete a clinical trial or return for post- treatment follow- up; • clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial; • **protocol deviations or non- compliance with GCP requirements, or other data integrity reasons, that cause us or the FDA or other regulatory authorities to exclude data from non- compliant sites or investigators, which may cause the trial to be underpowered to meet the endpoints; • delays by us or our CROs in qualifying or analyzing patient data at the completion of clinical trials; •** failure to demonstrate a benefit from using a ~~product~~ **drug** candidate; • addressing subject safety concerns that arise during the course of a clinical trial; • adding a sufficient number of clinical trial sites; or • obtaining sufficient ~~product~~ supply of ~~product~~ **drug** candidate for use in nonclinical studies or clinical trials from third- party suppliers. Further, conducting clinical trials in foreign countries, as we intend to do for our ~~product~~ **drug** candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the

utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our ~~product~~ **drug** candidates. If we experience delays in the completion of, or termination of, any clinical trial of our ~~product~~ **drug** candidates, the commercial prospects of our ~~product~~ **drug** candidates will be harmed, and our ability to generate product revenues from any of these ~~product~~ **drug** candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our ~~product~~ **drug** candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. If the results of our current and future clinical trials are inconclusive with respect to the efficacy of our ~~product~~ **drug** candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our ~~product~~ **drug** candidates, we may: • incur unplanned costs; • be delayed in or prevented from obtaining marketing approval for our ~~product~~ **drug** candidates; • obtain approval for indications or patient populations that are not as broad as intended or desired; • obtain approval with labeling that includes significant use or distribution restrictions or safety warnings including boxed warnings; • be subject to changes in the way the ~~product~~ **drug candidate** is administered; • be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; • have regulatory authorities withdraw their approval of the **drug** product or impose restrictions on its distribution in the form of a modified ~~risk evaluation and mitigation strategy, or~~ REMS; • be subject to the addition of labeling statements, such as warnings or contraindications; • be sued; or • experience damage to our reputation. Any " topline ", interim, initial, or 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. From time to time, we may publicly disclose preliminary or topline data from our nonclinical studies and clinical trials, which is based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or clinical 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 topline 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. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our nonclinical studies and clinical trials. For example, in October 2022 we announced that an independent **DMC** ~~data monitoring committee~~ had conducted an unblinded interim efficacy and futility analysis with respect to our Phase 2 / 3 LIFT- AD clinical trial. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. Additionally, we rely on data received from clinical trials, whether preliminary or final, to inform decisions on future clinical trials, including trial design, trial size, and whether or not to initiate additional clinical trials **(including any potential confirmatory or Phase 3 registrational trials)** . For example, in November 2020, we initiated ACT- AD, an exploratory Phase 2 clinical trial, to better understand the overall effects of fosgonimeton on working memory processing speed and cognitive measures. Topline results of ACT- AD were announced in June 2022. We used these data to help inform strategic decisions around LIFT- AD and expect to use these data to help inform strategic decisions in the future around current clinical trials and any additional trials that we may initiate. Topline results are based on a preliminary analysis of then- available data, and a more comprehensive and full review of the data may result in different conclusions, which could have a negative impact on our decisions regarding any additional trials for fosgonimeton. There is no assurance that the amendments to our ongoing LIFT- AD trial based on our findings from the ACT- AD trial and our interim analysis of the LIFT- AD trial will ultimately result in a successful trial. For example, our biomarker data may not translate into a statistically significant clinical benefit, the FDA may not agree with our statistical plan or analyses, or the trial may not be sufficiently powered for our endpoint measures. 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~~ **drug** candidate or ~~product~~ **drug** 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 interim, topline, 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~~ **drug** candidates may be harmed, which could harm our business, operating results, prospects or financial condition. If we experience delays or difficulties in the enrollment or retention of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our ~~product~~ **drug** candidates if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these clinical trials through completion of such trials as required by the FDA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. Patient enrollment may also be affected if our competitors have ongoing clinical trials for programs that are under development for the same indications as our ~~product~~ **drug** candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' programs. Additionally, publicly reported results of our completed clinical trials may impact enrollment of our trials in progress. If we are unable to

locate a sufficient number of such patients, our clinical trial and development plans could be delayed. If we are delayed or unsuccessful in enrolling the desired number of subjects in our trials, whether as a result of the outcomes of prior trials conducted by us, competing clinical trials, overly stringent eligibility requirements, or other factors, our clinical trial results could be delayed, the costs of our clinical trials could materially increase, and the overall development timeline for fosgonimeton could be negatively impacted. For example, enrollment in our ongoing clinical trials had slowed due to the effects of the COVID- 19 pandemic, including governmental restrictions imposed in Australia, where certain of our clinical trial sites are located. In our ACT- AD clinical trial, this slowed recruitment resulted in a change in the timing of topline results from our Phase 2 ACT- AD clinical trial, which were announced in June 2022. We cannot ensure that similar enrollment issues will not occur again in the future. Even if we are successful in enrolling the targeted number of subjects in our trials, the FDA and other regulators may request additional clinical trials with larger numbers of subjects **(including potential confirmatory or Phase 3 registrational trials)** as a condition to any regulatory approval. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Further, to the extent any of our clinical trial sites fail to comply with the approved study protocol, good clinical practices, or FDA regulations, we may be required to exclude such sites, participants such sites may have enrolled, as well as the data collected by such sites. If any of these events were to occur, or if we are required to exclude any data for any reason, we may be required to recruit more sites or more participants than we initially thought. Enrollment delays or other delays in our clinical trials may result in increased development costs for our ~~product~~ **drug** candidates and jeopardize our ability to obtain marketing approval for the sale of our ~~product~~ **drug** candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow- up periods. We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer, or less expensive than the ~~product~~ **drug** candidates we develop, our commercial opportunities will be negatively impacted. The biotechnology and pharmaceutical industries utilize rapidly advancing technologies and are characterized by intense competition. While we believe that our scientific knowledge, platform technology and development expertise provide us with competitive advantages, we face competitive pressures from both large and small pharmaceutical companies, emerging biotechnology companies, as well as academic, government and private research institutions. Many of our competitors have access to greater financial resources, market presence, expertise in development, preclinical and clinical testing, manufacturing, commercialization, regulatory approval process, or marketing and sales than we do. Our competitors may compete with us in patient recruitment, clinical research organization, and operational resources. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do. ~~Product~~ **Drug** candidates that we may successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. For example, the FDA recently granted ~~accelerated~~ **traditional** approval for lecanemab, a drug developed by Biogen Inc. and Eisai Co., Ltd., and Eli Lilly and Company is also developing ~~product~~ **drug** candidates for **AD** ~~Alzheimer' s disease~~ . Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety and convenience of our **drug** products. Our competitors may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our ~~product~~ **drug** candidates. The availability of reimbursement from government and other third- party payors will also significantly affect the pricing and competitiveness of our **drug** products **. For example, CMS announced a two- part National Coverage Determination, or NCD, under which Medicare will cover monoclonal antibodies that target amyloid (or plaque) for the treatment of AD that receive traditional approval from the FDA under coverage with evidence development. Additionally, for drugs that FDA has not determined to have shown a clinical benefit or that received an accelerated approval, Medicare will provide coverage in FDA or NIH approved clinical trials. In June 2023, CMS announced that Medicare will cover new Alzheimer' s drugs with traditional FDA approval when a physician and clinical team participate in CMS' registry to collect evidence about how these drugs work in the real world. Current and future CMS coverage restrictions on classes of drugs that encompass our drug candidates could have a material adverse impact on our ability to commercialize our drug candidates, if approved, generate revenue and attain profitability. It is unclear how future CMS coverage decisions and policies will impact our business** . Our competitors may also 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. For additional information regarding our competition, see the section **of this report** titled " Part I, Item 1 – Business — Competition " ~~in this report~~ . We may expend our limited resources to pursue a particular ~~product~~ **drug** candidate or indication and fail to capitalize on ~~product~~ **drug** 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 focus on research programs, therapeutic platforms and ~~product~~ **drug** candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other therapeutic platforms or ~~product~~ **drug** candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs, therapeutic platforms and ~~product~~ **drug** 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~~ **drug** candidate, we may relinquish valuable rights to that ~~product~~ **drug** 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. We may develop ~~product~~ **drug** candidates in combination with other therapies, which exposes us to additional risks. We may develop ~~product~~ **drug** candidates in combination with one or more other approved or unapproved therapies. Even if any ~~product~~ **drug** candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable foreign

regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our **drug** product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our ~~product~~ **drug** candidates are replaced as the standard of care for the indications we choose for any of our ~~product~~ **drug** candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own **drug** products, if approved, being removed from the market or being less successful commercially. We also may choose to evaluate ~~product~~ **drug** candidates in combination with one or more therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell any ~~product~~ **drug** candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our **drug** product. In addition, unapproved therapies face the same risks described with respect to our ~~product~~ **drug** candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval. If the FDA or comparable foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our ~~product~~ **drug** candidate we develop, we may be unable to obtain approval of or market such combination therapy. Our long- term prospects depend in part upon discovering, developing and commercializing additional ~~product~~ **drug** candidates, which may fail in development or suffer delays that adversely affect their commercial viability. Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize ~~product~~ **drug** candidates beyond those we currently have in clinical and nonclinical development. A ~~product~~ **drug** candidate can unexpectedly fail at any stage of nonclinical and clinical development. The historical failure rate for ~~product~~ **drug** candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from nonclinical testing or early clinical trials of a ~~product~~ **drug** candidate may not be predictive of the results that will be obtained in later stage clinical trials of the ~~product~~ **drug** candidate. The success of other future ~~product~~ **drug** candidates we may develop will depend on many factors, including the following: • generating sufficient data to support the initiation or continuation of clinical trials; • obtaining regulatory permission to initiate clinical trials; • contracting with the necessary parties to conduct clinical trials; • successful enrollment of patients in, and the completion of, clinical trials on a timely basis; • the timely manufacture of sufficient quantities of the ~~product~~ **drug** candidate for use in clinical trials; and • adverse events in the clinical trials. Even if we successfully advance any other future ~~product~~ **drug** candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this " Risk Factors " section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our other future ~~product~~ **drug** candidates. We have conducted certain research and development operations through our Australian wholly owned subsidiary. If we lose our ability to operate in Australia, or if our subsidiary is unable to receive the research and development tax credit allowed by Australian regulations, our business and results of operations could suffer. In July 2020, we formed a wholly owned Australian subsidiary to conduct various preclinical and clinical activities for our **drug** product and development candidates in Australia. Due to the geographical distance and lack of employees currently in Australia, as well as our lack of experience operating in Australia, we may not be able to efficiently or successfully monitor, develop and commercialize our ~~lead~~ **drug** ~~products~~ **product and development candidates** in Australia, including conducting clinical trials. Furthermore, we have no assurance that the results of any clinical trials that we conduct for our ~~product~~ **drug** candidates in Australia will be accepted by the FDA or foreign regulatory authorities for development and commercialization approvals. In addition, current Australian tax regulations provide for a refundable research and development tax credit equal to 43. 5 % of qualified expenditures. If we lose our ability to operate our subsidiary in Australia, or if we are ineligible or unable to receive the research and development tax credit, or the Australian government significantly reduces or eliminates the tax credit, our business and results of ~~operation~~ **operations** may be adversely affected. The loss of any of our key personnel could significantly harm our business, results of operations and competitive position. In order to compete, we must attract, retain, and motivate executives and other key employees. Hiring and retaining qualified executives, scientists, technical and legal and accounting staff are critical to our business, and competition for experienced employees in our industry can be ~~intense~~ **high** . The loss of one or more of these key employees, or our inability to hire additional key personnel when needed, could have a material adverse effect on our business and prospects. Risks Relating to ~~COVID- 19 and Other~~ Health Epidemics The ~~continuing and~~ potential effects of **health epidemics** ~~the novel coronavirus disease, or COVID- 19, pandemic and other disease outbreaks~~ could adversely impact our business, including our nonclinical studies and clinical trials. **Our** ~~The COVID- 19 pandemic and government measures taken in response had a significant impact, both direct and indirect, on businesses and~~ **business** ~~and commerce, including worker shortages, supply chain disruptions, facility and production suspensions, and fluctuations in demand for certain goods and services, such as medical services and supplies. In response to the spread of COVID- 19, we temporarily closed our executive offices and limited the number of staff in our research and development laboratory spaces. While at this time our offices and laboratory spaces have been reopened at full capacity, a resurgence in cases of COVID- 19 or another disease outbreak~~ could ~~occur,~~ **in the future be adversely impacted by the effects of possible health epidemics and other outbreaks** which could cause ~~us to again close down our facilities or take other measures in response. In particular, new and highly contagious variants of COVID - 19 could continue to emerge and spread quickly throughout certain areas of the United States and elsewhere, and at this point we are unable to determine when and to what extent any such resurgence will affect our business. In addition, a number of our clinical trial sites have in the past been and could in the future be subject to restrictions related to COVID- 19 that adversely affect their operations. While COVID- 19- related restrictions have been eased in many of our clinical trial sites, new restrictions could in the future be imposed, whether in response to an outbreak of a new variant of COVID- 19 or any similar outbreak. While the extent of the continuing impact of the COVID- 19 pandemic on our business and financial results is uncertain, a surge in cases of COVID- 19~~

~~or diseases could have a material negative impact on our business, financial condition and operating results. We may in the future experience~~ disruptions that could severely impact our business, nonclinical studies and clinical trials ~~as a result of the COVID- 19 pandemic or other disease outbreaks~~. Such disruptions may include: • delays or difficulties in enrolling and retaining patients in our clinical trials, particularly elderly subjects, who may be at a higher risk of severe illness or death, which can be further complicated by the presence of comorbidities that are often present in AD subjects; • difficulties interpreting data from our clinical trials due to the possible effects of such diseases on cognition of the subjects enrolled in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; • interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non- essential), which may impact the integrity of subject data and clinical study endpoints; • interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines; • interruption of, or delays in receiving, supplies of our ~~product~~ **drug** candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; • interruptions in nonclinical studies due to restricted or limited operations at our laboratory facility; • limitations on employee resources that would otherwise be focused on the conduct of our nonclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; • interruptions, difficulties or delays arising in our existing operations and company culture as a result of some or all of our employees working remotely; • interruption or delays to our sourced discovery and clinical activities; and • changes in clinical site procedures and requirements as well as regulatory requirements for conducting clinical trials during the pandemic. ~~In~~ **For example, in** the event of a **disease outbreak or** resurgence of COVID- 19 ~~or the emergence of new disease outbreaks~~, we could be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from such diseases **. On May 11, 2023, the federal government ended the COVID- 19 public health emergency, which ended a number of temporary changes made to federally funded programs while some continue to be in effect**. Since March 2020, the FDA has issued various COVID- 19 related guidance documents for sponsors and manufacturers, ~~including guidance on conducting clinical trials during~~ **many of which have expired or were withdrawn with** the **expiration of** ~~pandemic, and guidance on good manufacturing practice considerations among others. Recently, President Biden announced that the administration intends to end~~ the COVID- 19 ~~national and~~ public health ~~emergencies~~ **emergency declaration** ~~on May 11~~, ~~2023~~ **although some COVID- 19 related guidance documents continue in effect**. The full impact of ~~the~~ **this** termination **of the national emergency and the wind- down** of the public health ~~emergencies~~ **emergency** on FDA and other regulatory policies and operations ~~are~~ **is** unclear. The trading prices for shares of biopharmaceutical companies have in the past been and could in the future be highly volatile as a result of **health epidemics, including** the COVID- 19 pandemic ~~or other disease outbreaks~~, and the trading prices for shares of our common stock could also experience high volatility. In the event of **an emergence of new disease outbreaks or** a resurgence of COVID- 19 ~~or the emergence of new disease outbreaks~~, we could face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from ~~the spread~~ **a health epidemic, including a resurgence** of COVID- 19 **,** could materially and adversely affect our business and the value of our common stock. The ultimate impact of a **possible health epidemic or other outbreak, including a** resurgence of COVID- 19 **,** ~~or other disease outbreaks~~ on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted. In addition, our business could be significantly adversely affected by other business disruptions to us or our third- party providers that could seriously harm our potential future revenue and financial condition and increase our costs and expenses. Our operations, and those of our CROs, commercial manufacturing organizations, or CMOs, and other contractors, consultants, and third parties could be subject to other global pandemics, earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man- made disasters or business interruptions, for which we are predominantly self- insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third- party manufacturers to produce and process our ~~product~~ **drug** candidates. Our ability to obtain clinical supplies of our ~~product~~ **drug** candidates could be disrupted if the operations of these suppliers are affected by a man- made or natural disaster or other business interruption. Risks Relating to Our Financial Position and Capital Needs We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have not generated any revenue from **drug** product sales and our ~~product~~ **drug** candidates will require substantial additional investment before they may provide us with any revenue. We had net losses of $ **117. 7 million and $** 95. 6 ~~million and $ 54. 9~~ million for the years ended December 31, **2023 and** 2022 ~~and 2021~~, respectively, and an accumulated deficit of $ ~~191~~ **309** . ~~5~~ **2** million as of December 31, ~~2022~~ **2023** . We have devoted most of our financial resources to research and development, including our clinical and nonclinical development activities. To date, we have financed our operations primarily with proceeds from the sale and issuance of common stock, convertible preferred stock, common stock warrants, and convertible notes, and to a lesser extent from grant income and stock option exercises. We expect to incur significant expenses and increasing operating losses for the foreseeable future as we: • continue our research and nonclinical and clinical development of our ~~product~~ **drug** candidates; • expand the scope of our clinical studies for our current and prospective ~~product~~ **drug** candidates; • initiate additional nonclinical, clinical or other studies for our ~~product~~ **drug** candidates, including any potentially pivotal trials with respect to fosgonimeton for the treatment of mild- to- moderate AD in addition to LIFT- AD, and **continue** ~~further extend~~ the open label extension of the ACT- AD and LIFT- AD trials; • change or add additional manufacturers or suppliers and manufacture drug supply and drug product

for clinical trials and commercialization; • seek regulatory and marketing approvals for any of our ~~product~~ **drug** candidates that successfully complete clinical trials; • attract, hire and retain additional personnel; • operate as a public company; • continue to expand our facilities and lab space; • seek to identify and validate additional ~~product~~ **drug** candidates; • acquire or in- license other ~~product~~ **drug** candidates and technologies or engage in other strategic transactions; • make milestone or other payments under our in- license or other agreements; • maintain, protect and expand our intellectual property portfolio; • establish a sales, marketing and distribution infrastructure to commercialize any **drug** products for which we may obtain marketing approval; • create additional infrastructure to support our operations and our **drug** product development and planned future commercialization efforts; • incur expenses in connection with legal proceedings, and addressing potential stockholder activism; and • experience any delays or encounter issues with any of the above. Our expenses could increase beyond expectations for a variety of reasons, including if we are required by the FDA, the European Medicines Agency, or EMA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity. We will require substantial additional funding to finance our operations, complete the development and commercialization of fosgonimeton, and develop and commercialize other and future ~~product~~ **drug** candidates. If we are unable to raise this funding when needed, we may be forced to delay, reduce, or eliminate our **drug** product development programs or other operations. Since our inception, we have used substantial amounts of cash to fund our operations, and we expect our expenses to increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, fosgonimeton. Developing fosgonimeton and conducting clinical trials for the treatment of AD, PDD, DLB, and any other indications that we may pursue in the future will require substantial amounts of capital. In addition, if we obtain marketing approval for fosgonimeton or any future ~~product~~ **drug** candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing, and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. As of December 31, ~~2022~~ **2023** , we had cash, cash equivalents and investments of $ ~~245~~ **147** . ~~2~~ **4** million. Based upon our current operating plan, we estimate that our existing cash, cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months following the date of this report. However, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate. The amount and timing of our future funding requirements depends on many factors, some of which are outside of our control, including but not limited to: • the progress, costs, clinical trial design, results of and timing of our LIFT- AD trial and other clinical trials of fosgonimeton, including for potential additional indications that we are pursuing beyond AD, such as PDD, DLB, and **the continuation** ~~a potential further extension~~ of the open label extension of the ACT- AD and LIFT- AD trials; • the willingness of the FDA and EMA to accept our LIFT- AD trial, as well as data from our completed and planned clinical and nonclinical studies and other work, as the basis for review and approval of fosgonimeton for AD and the potential need for additional clinical trials **(including potential confirmatory or Phase 3 registrational trials)** ; • the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals; • the number and characteristics of ~~product~~ **drug** candidates that we pursue; • our ability to manufacture sufficient quantities of our ~~product~~ **drug** candidates; • our need to expand our research and development activities; • the costs associated with securing and establishing commercialization and manufacturing capabilities; • the costs of acquiring, licensing or investing in businesses, ~~product~~ **drug** candidates and technologies; • the cost, timing and outcomes of any litigation involving our company, including securities class actions and government investigations which we may be or may in the future become involved in; • our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights; • our need and ability to retain management and hire scientific, clinical and other personnel; • the effect of competing drugs and ~~product~~ **drug** candidates and other market developments; • our need to implement additional internal systems and infrastructure, including financial and reporting systems; and • the economic and other terms, timing of and success of any collaboration, licensing or other arrangements into which we may enter in the future. In January 2023, we entered into a sales agreement with Cantor Fitzgerald & Co., or Cantor Fitzgerald, and BTIG, LLC, or BTIG, to sell shares of our common stock having aggregate sales proceeds of up to $ 75. 0 million, from time to time, through an at- the- market, or ATM, equity offering program under which Cantor **Fitzgerald** and BTIG are acting as sales agents. We have not sold any securities pursuant to this ATM offering. However, additional funding may not be available to us on acceptable terms or at all. Any such funding may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail or abandon one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or ~~product~~ **drug** candidates or otherwise agree to terms unfavorable to us **. We expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. In addition, we may seek additional capital to take advantage of favorable market conditions or strategic opportunities even if we believe we have sufficient funds for our current or future operating plans. Based on our research and development plans, we expect that our existing cash, cash equivalents and investments will enable us to fund our operations for at least 12 months following the date of this report. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Our**

ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. For example, the current inflationary economic environment, health epidemics, and rising interest rates have resulted in a disruption of global financial markets. If the disruption persists or deepens, we could be unable to access additional capital, which could negatively affect our ability to consummate certain corporate development transactions or other important, beneficial or opportunistic investments. If additional funds are not available to us when we need them, on terms that are acceptable to us, or at all, we may be required to take steps that could adversely impact our business, including delaying, limiting, reducing or terminating nonclinical studies, clinical trials or other research and development activities or eliminating one or more of our development programs altogether, or delaying, limiting or reducing or terminating efforts to prepare for commercialization of any future approved drug products. We currently have a shelf registration statement effective and an existing ATM equity offering program, however, our ability to raise capital under this registration statement and through our ATM equity offering program may be limited by, among other things, SEC rules and regulations impacting the eligibility of smaller companies to use Form S- 3 for primary offerings of securities . Adverse events or perceptions affecting the financial services industry could adversely affect our operating results, liquidity, financial condition and prospects. Limited liquidity, defaults, non- performance or other adverse developments affecting financial institutions or parties with which we do business, or perceptions regarding these or similar risks, have in the past and may in the future lead to market- wide liquidity problems. For example, ~~on~~ **in** March ~~10,~~ 2023, Silicon Valley Bank, or SVB, was closed and placed in receivership and subsequently, additional financial institutions have been placed into receivership. We did not hold cash deposits or other accounts with SVB and did not, and as of the date of this report do not, otherwise have a direct business relationship with SVB or similarly situated financial institutions. However, companies that did have a business relationship with SVB faced: • delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; • loss of access to revolving existing credit facilities or other working capital sources or the inability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources; • potential or actual breach of obligations, including U. S. federal and state wage laws and contracts that required them to maintain letters or credit or other credit support arrangements; and • termination of cash management arrangements or delays in accessing or actual loss of funds subject to cash management arrangements. As a result of U. S. government intervention, account holders subsequently regained access to their accounts, including the uninsured portion of deposit accounts; however, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB and similarly situated financial institutions **were** ~~may be~~ unable to access to such sources of liquidity. There is no guarantee that the U. S. government will intervene to provide access to uninsured funds in the future in the event of the failure of other financial institutions, or that they would do so in a timely fashion. In such an event, parties with which we have commercial agreements may be unable to satisfy their obligations to, or enter into new commercial arrangements with, us. Concerns regarding the U. S. or international financial systems could impact the availability and cost of financing, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any of these risks could materially impact our operating results, liquidity, financial condition and prospects. **The value of our investments is subject to significant capital markets risk related to changes in interest rates and credit spreads as well as other investment risks, which may adversely affect our operating results, liquidity, financial condition and prospects. Our results of operations are affected by the performance of our investment portfolio. Our excess cash is invested by an external investment management service provider, under the direction of our management in accordance with our investment policy. The investment policy defines constraints and guidelines that restrict the asset classes that we may invest in by type, duration, quality and value. Our investments are subject to market- wide risks, and fluctuations, as well as to risks inherent in particular securities. The failure of any of the investment risk strategies that we employ could have a material adverse effect on our operating results, liquidity, financial condition and prospects. The value of our investments is exposed to capital market risks, and our results of operations, liquidity, financial condition or cash flows could be adversely affected by realized losses, impairments and changes in unrealized positions as a result of: significant market volatility, changes in interest rates, changes in credit spreads and defaults, a lack of pricing transparency, a reduction in market liquidity, declines in equity prices, changes in national, state / provincial or local laws and the strengthening or weakening of foreign currencies against the U. S. dollar. Levels of write- down or impairment are impacted by our assessment of the intent to sell securities that have declined in value as well as actual losses as a result of defaults or deterioration in estimates of cash flows. If we reposition or realign portions of the investment portfolio and sell securities in an unrealized loss position, we will incur realized losses. Any such charge may have a material adverse effect on our results of operations and business.** Our ability to use net operating losses to offset future taxable income may be subject to certain limitations. As of December 31, ~~2022~~ **2023** , we had federal net operating loss carryforwards, or NOLs, to offset future taxable income of approximately $ 9. 5 million and federal tax credit carryforwards of approximately $ ~~5~~ **12** . ~~6~~ **4** million, which expire over a period of ~~9~~ **8** to ~~15~~ **14** years. Federal NOLs of $ ~~104~~ **138** . ~~4~~ **7** million were generated after 2017, and therefore do not expire. At December 31, ~~2022~~ **2023** , we also had state NOLs of $ ~~2~~ **3** . ~~7~~ **3** million, which expire over a period of ~~19~~ **18** to 20 years. A lack of future taxable income would adversely affect our ability to utilize these NOLs. In addition, under Section 382 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 NOLs to offset future taxable income. We may have already experienced one or more ownership changes. Depending on the timing of any future utilization of our NOLs and tax credit carryforwards, we may be limited as to the amount that can be utilized each year as a result of such previous ownership changes. However, we do not believe such limitations will cause our NOL and tax credit carryforwards to expire unutilized. In addition, future changes in our stock ownership as well as other changes that may be outside of our control, could result in additional ownership changes under Section 382 of the Code. Our NOLs may also be impaired under similar provisions of state law or limited pursuant to provisions of the Tax Cuts and Jobs Act amendments to the

Code, as modified by the Coronavirus Aid, Relief, and Economic Security Act. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets. Changes in tax laws could have a material adverse effect on our business, cash flows, results of operations or financial condition. We are subject to the tax laws, regulations, and policies of several taxing jurisdictions. Changes in tax laws, as well as other factors, could cause us to experience fluctuations in our tax obligations and effective tax rates and otherwise adversely affect our tax positions or our tax liabilities. For example, many countries and local jurisdictions and organizations such as the Organization for Economic Cooperation and Development have proposed or implemented new tax laws or changes to existing tax laws, including additional taxes on payroll or employees. Any new or changes to tax laws could adversely affect our effective tax rate, operating results, tax credits or incentives or tax payments, which could have a material adverse effect on our business, cash flows, results of operations or financial condition. Risks Relating to Regulatory Approval and Other Legal Compliance Matters The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our ~~product~~ **drug** candidates, we will not be able to commercialize, or will be delayed in commercializing, our ~~product~~ **drug** candidates, and our ability to generate revenue will be materially impaired. Our ~~product~~ **drug** candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. Before we can commercialize any of our ~~product~~ **drug** candidates, we must obtain marketing approval. Obtaining approval by the FDA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Further, securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval for our ~~product~~ **drug** candidates, the FDA and other comparable foreign regulatory authorities may approve our ~~product~~ **drug** candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the **drug** product' s commercial potential. We have not submitted for, or obtained, regulatory approval for any ~~product~~ **drug** candidate, and it is possible that none of our ~~product~~ **drug** candidates will ever obtain regulatory approval. Further, development of our ~~product~~ **drug** candidates or regulatory approval may be delayed for reasons beyond our control. Applications for our ~~product~~ **drug** candidates could fail to receive regulatory approval for many reasons, including the following: • the FDA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials; • the FDA or other comparable foreign regulatory authorities may determine that our ~~product~~ **drug** candidates are not safe and effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use; • the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval; • the FDA or other comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials; • we may be unable to demonstrate to the FDA or other comparable foreign regulatory authorities that our ~~product~~ **drug** candidate' s risk- benefit ratio for its proposed indication is acceptable; • the FDA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval or resulting in delays in our regulatory approval, including, for example, legislation or agency policies that aim to reform the accelerated approval process and FDA' s increased scrutiny of post- approval confirmatory studies, which can result in withdrawal of accelerated approval if such studies fail to confirm a clinical benefit. This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our ~~product~~ **drug** candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we obtain approval of our ~~product~~ **drug** candidates, regulatory authorities may approve any of our ~~product~~ **drug** candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a ~~risk evaluation and mitigation strategy, or~~ REMS. Regulatory authorities may not approve the price we intend to charge for **drug** products we may develop, may grant approval contingent on the performance of costly post- marketing clinical trials, or may approve a ~~product~~ **drug** candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that ~~product~~ **drug** candidate. Any of the foregoing scenarios could seriously harm our business. Of the large number of drugs in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval processes as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our ~~product~~ **drug** candidates, which would significantly harm our business, results of operations and prospects. Our current or future ~~product~~ **drug** candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could inhibit regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences. As is the case with pharmaceuticals generally, it is likely that there may be side

effects and adverse events associated with our ~~product~~ **drug** candidates' use. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our ~~product~~ **drug** candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug- related side effects could affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. If our ~~product~~ **drug** candidates are associated with undesirable side effects or have unexpected characteristics in nonclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective. Treatment- related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the clinical trial, or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected ~~product~~ **drug** candidate and may harm our business, financial condition and prospects significantly. Patients in our clinical trials may in the future suffer significant adverse events or other side effects not observed in our nonclinical studies or previous clinical trials. Some of our ~~product~~ **drug** candidates may be used as chronic therapies or be used in populations for which safety concerns may be particularly scrutinized by regulatory agencies. In addition, if our ~~product~~ **drug** candidates are used in combination with other therapies, our ~~product~~ **drug** candidates may exacerbate adverse events associated with the therapy. Patients treated with our ~~product~~ **drug** candidates may also be undergoing separate treatments which can cause side effects or adverse events that are unrelated to our ~~product~~ **drug** candidate, but may still impact the success of our clinical trials, including, for example, by interfering with the effects of our ~~product~~ **drug** candidates. A pre- specified group analysis of patients in our ACT- AD clinical trial identified a potential diminished effect of the combination of standard- of- care (AChEIs) and fosgonimeton. While more clinical studies are needed to determine the safety and efficacy of fosgonimeton, to the extent standard- of- care AChEIs impact the effects of fosgonimeton and if a significant portion of the patient population has already been treated with AChEIs, the potential target patient population or the indication we seek for fosgonimeton may be significantly smaller than we had anticipated, which could materially harm our business and prospects. The inclusion of elderly patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using. If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our clinical trials, or we may be required to abandon the clinical trials or our development efforts of that ~~product~~ **drug** candidate altogether. We, the FDA other comparable regulatory authorities or an IRB may suspend clinical trials of a ~~product~~ **drug** candidate at any time for various reasons, including a belief that subjects in such clinical trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early- stage clinical trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the ~~product~~ **drug** candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects. Further, if any of our ~~product~~ **drug** candidates obtains marketing approval, toxicities associated with such ~~product~~ **drug** candidates and not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the **drug** product or the withdrawal of the **drug** product from the market. We cannot predict whether our ~~product~~ **drug** candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on nonclinical studies or early-stage clinical trials. Obtaining and maintaining regulatory approval of our ~~product~~ **drug** candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our ~~product~~ **drug** candidates in other jurisdictions. Obtaining and maintaining regulatory approval of our ~~product~~ **drug** candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA grants marketing approval of a ~~product~~ **drug** candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the ~~product~~ **drug** candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional nonclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a ~~product~~ **drug** candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our **drug** products is also subject to approval. We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of ~~product~~ **drug** candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our **drug** products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential ~~product~~ **drug** candidates will be harmed. Even if we receive regulatory approval of our ~~product~~ **drug** 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~~ **drug** candidates. Any regulatory approvals that we receive for our ~~product~~ **drug** candidates will

require surveillance to monitor the safety and efficacy of the ~~product~~ **drug** candidate. The FDA may also require a REMS in order to approve our ~~product~~ **drug** candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our ~~product~~ **drug** candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our ~~product~~ **drug** candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as continued compliance with ~~current good manufacturing practice, or~~ cGMP regulations, ~~good laboratory practice, or~~ GLP ~~,~~ regulations and ~~good clinical practice, or~~ GCP regulations ~~,~~ for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our ~~product~~ **drug** candidates, 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 result in, among other things: • restrictions on the marketing or manufacturing of our ~~product~~ **drug** candidates, withdrawal of the **drug** product from the market or voluntary or mandatory product recalls; • manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation; • revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings; • imposition of a REMS, which may include distribution or use restrictions; • requirements to conduct additional post- market clinical trials to assess the safety of the **drug** product; • fines, warning letters or holds on clinical trials; • refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals; • product seizure or detention, or refusal to permit the import or export of our ~~product~~ **drug** candidates; and • 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~~ **drug** candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. It is difficult to predict how current and future legislation, executive actions, and litigation, including the executive orders, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA' s and other agencies' ability to exercise their regulatory authority, including FDA' s pre- approval inspections and timely review of any regulatory filings or applications we submit to the FDA. To the extent any executive actions impose constraints on FDA' s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. **In addition, if the Supreme Court reverses or curtails the Chevron doctrine, which gives deference to regulatory agencies in litigation against FDA and other agencies, more companies may bring lawsuits against FDA to challenge longstanding decisions and policies of FDA, which could undermine FDA' s authority, lead to uncertainties in the industry, and disrupt FDA' s normal operations, which could delay FDA' s review of our marketing applications.** Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product' s approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses, and a company that is found to have improperly promoted off- label uses may be subject to significant civil, criminal and administrative penalties. The occurrence of any event or penalty described above may inhibit our ability to commercialize our ~~product~~ **drug** candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity. Disruptions at the FDA, the **SEC** ~~Securities and Exchange Commission~~ and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain 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, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA' s ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the ~~Securities and Exchange Commission, or the~~ SEC, and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. **To** ~~Disruptions at the FDA and other~~ -- **the extent** ~~agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, in 2018 and 2019, the U. S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Separately, in response to the COVID- 19 public health emergency, since March 2020 when foreign and domestic inspections facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre- approval inspections on a prioritized basis. In 2020 and 2021, a number of companies announced receipt of complete response letters due to~~ the FDA' s ~~inability to complete required inspections~~ **normal operations are disrupted or delayed,** for **example** ~~their applications. While the FDA has largely caught up with domestic preapproval inspections, it continues to work through its backlog of foreign inspections. However, the FDA may not be able to continue its current inspection pace, and review timelines could be extended, including where a pre- approval inspection or an inspection of clinical sites is required and~~ due to ~~the ongoing COVID- 19 pandemic,~~ travel restrictions, **public health** or **geopolitical issues,** staffing shortages, **or lack of funding,** the FDA ~~is~~ **may not be** ~~unable~~ -- **able** to complete ~~such required~~ **the necessary** inspections **or provide feedback in a timely manner** during ~~the~~ **our clinical**

development or review period. **If any such** ~~Regulatory authorities outside the U. S. may adopt similar restrictions or other policy measures in response to the COVID- 19 pandemic and may experience~~ delays ~~in their regulatory activities. If a prolonged government shutdown~~ or ~~other disruption~~ **disruptions were to** ~~occurs~~ **occur** ~~, or if global health or other concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities in a timely manner~~, 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. Further, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways. If we are unable to obtain such approval, we may be required to conduct additional nonclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous postmarketing requirements, the FDA may seek to withdraw accelerated approval. We may ~~in the future~~ seek an accelerated approval for ~~our~~ one or more of our ~~product~~ **drug** 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 or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor' s agreement to conduct, in a diligent manner, additional post- approval confirmatory studies to verify and describe the drug' s clinical benefit. If such post- approval studies fail to confirm the drug' s clinical benefit, the FDA may withdraw its approval of the drug. Prior to seeking accelerated approval for any of our ~~product~~ **drug** candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or receive an expedited regulatory designation (e. g., breakthrough therapy designation) for our ~~product~~ **drug** candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our ~~product~~ **drug** candidate would result in a longer time period to commercialization of such ~~product~~ **drug** candidate, could increase the cost of development of such ~~product~~ **drug** candidate and could harm our competitive position in the marketplace. Further, to the extent the FDA materially changes its policies or regulatory requirements with respect to the accelerated approval program or its internal review process for such program, our clinical development plans and regulatory approval under such program could be materially impacted or delayed. ~~In view of the recent controversy regarding the FDA' s approval of Biogen' s Aduhelm, a biologic, through the accelerated approval pathway, the FDA has requested the Office of the Inspector General to investigate the FDA' s review of Aduhelm leading up to its approval~~ On December 29, 2022, the Consolidated Appropriations Act, 2023, including the ~~Food and Drug Omnibus Reform Act (~~FDORA ~~)~~, was signed into law. FDORA made several changes to the FDA' s authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post- approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non- compliance with post- approval requirements. It is unclear how these proposals, future policy changes, and changes in FDA regulation will impact new drug applications in the treatment of **AD** ~~Alzheimer' s disease~~ and our clinical development programs. We may face difficulties from changes to current regulations and future legislation. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations. The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our ~~product~~ **drug** candidates or any future ~~product~~ **drug** candidates, restrict or regulate post- approval activities and affect our ability to profitably sell a **drug** product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: • changes to our manufacturing arrangements; • additions or modifications to **drug** product labeling; • the recall or discontinuation of our **drug** products; or • additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ~~Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively,~~ ACA ~~,~~was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U. S. pharmaceutical industry. The ACA contained provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid

managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the U. S. Department of Health and Human Services Secretary, or HHS Secretary, as a condition for states to receive federal matching funds for the manufacturer' s outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extending the rebate program to individuals enrolled in Medicaid managed care organizations. The ACA also established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70 % (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) 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. In December 2020, the U. S. Centers for Medicare & Medicaid Services, or CMS, issued a final rule implementing significant manufacturer price reporting changes under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value- based purchasing arrangements. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. As discussed above, since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. On January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. In June 2021, the United States Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case without specifically ruling on the constitutionality of the ACA. Further, on August 16, 2022, President Biden signed the ~~Inflation Reduction Act of 2022, or~~ IRA ~~,~~ into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how additional challenges and healthcare reform measures of the Biden administration will impact the ACA. Complying with any new legislation and regulatory requirements could be time- intensive and expensive, resulting in a material adverse effect on our business. The Bipartisan Budget Act of 2018 also amended the ACA, effective January 1, 2019, by increasing the point- of- sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the " donut hole. " CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS has published a final rule to give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. The American Taxpayer Relief Act of 2012, or ATRA, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Other legislative changes include aggregate reductions to Medicare payments to providers of up to 2 % per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through ~~2031~~ **2032** with the exception of a temporary suspension implemented under various COVID-19 relief legislation ~~from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments can vary from 1 % in 2022 to up to 4 % in the final fiscal year of this sequester~~ . There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U. S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, in July 2021, the Biden administration released an executive order, " Promoting Competition in the American Economy, " with multiple provisions aimed at increasing competition for prescription drugs. In August 2022, Congress passed the IRA, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high- priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes. Further, the Biden administration released an additional executive order on October 14, 2022, directing the U. S. Department of Health and Human Services, or HHS, to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. **Various industry stakeholders, including pharmaceutical companies, the U. S. Chamber of Commerce, the National Infusion Center Association, the Global Colon Cancer Association, and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of IRA are unconstitutional.** The impact of these **judicial challenges as well as other** legislative, executive, and administrative actions and any future healthcare measures and agency

rules implemented by the **government** ~~Biden administration~~ on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our ~~product~~ **drug** candidates if approved. In April 2022, CMS released a finalized national policy for coverage of aducanumab, or Aduhelm, and any future monoclonal antibodies directed against amyloid approved by the FDA with an indication for use in treating **AD** ~~Alzheimer' s disease~~. According to the two- part ~~National Coverage Determination, or~~ NCD, Medicare will cover monoclonal antibodies that target amyloid (or plaque) for the treatment of **AD** ~~Alzheimer' s disease~~ that receive traditional approval from the FDA when furnished in accordance with the coverage criteria specified under coverage with evidence development. CMS will also provide enhanced access and coverage for Medicare patients participating in CMS- approved studies, such as data collection through routine clinical practice or registries. Additionally, for drugs that FDA has not determined to have shown a clinical benefit or that received an accelerated approval, Medicare will provide coverage in FDA or **NIH** ~~National Institutes of Health~~ approved clinical trials. ~~If~~ **In June 2023,** CMS ~~adopts similar~~ **announced that Medicare will** ~~coverage~~ --- **cover new** ~~restrictions for other classes of FDA- approved drugs for the treatment of~~ Alzheimer' s ~~disease~~ **drugs with traditional FDA approval when a physician and clinical team participate in CMS' registry to collect evidence about how these drugs work in the real world. Current and future CMS coverage restrictions on classes of drugs** that encompass our ~~product~~ **drug** candidates ~~,~~ **could have a material adverse impact on** our ability to commercialize our ~~product~~ **drug** candidates, if approved, generate revenue and attain profitability ~~could be negatively impacted~~. It is unclear how future CMS coverage decisions and policies will impact our business. At the state level, individual states are increasingly aggressive 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. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our **drug** products, once approved, or put pressure on our **drug** product pricing. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our **drug** products **. Further, FDA recently authorized the state of Florida to import certain prescription drugs from Canada for a period of two years to help reduce drug costs, provided that Florida' s Agency for Health Care Administration meets the requirements set forth by the FDA. Other states may follow Florida** . We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our ~~product~~ **drug** candidates or additional pricing pressures. Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition. There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare or impose price controls may adversely affect: • the demand for our ~~product~~ **drug** candidates, if we obtain regulatory approval; • our ability to set a price that we believe is fair for our **drug** products; • our ability to obtain coverage and reimbursement approval for a **drug** product; • our ability to generate revenue and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. We expect that other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved **drug** product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our ~~product~~ **drug** candidates. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure to what extent the trajectory of these legislative and regulatory proposals will be implemented by the federal and state governments, whether additional legislative changes will be enacted, whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our ~~product~~ **drug** candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. Our relationships with healthcare professionals, clinical investigators, CROs and third party payors in connection with our current and future business activities, and our participation in the federal health care programs and acceptance of federal grant funding, such as funding from the **NIH** ~~National Institutes of Health~~ , may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, which could expose us to, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings. Healthcare providers and third- party payors play a primary role in the recommendation and prescription of any ~~product~~ **drug** candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs,

third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our **drug** products for which we obtain marketing approval. Similarly, our participation in the federal health care programs and acceptance of federal grant funding from the NIH may subject us to federal false claims laws, civil penalties and assessments, criminal prosecution, and other administrative, civil, and criminal remedies. The laws that may affect our ability to operate include, but are not limited to: • the federal Anti- Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, 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 a federal healthcare program, such as the Medicare and Medicaid programs. 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. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act, or FCA. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection. • federal civil and criminal false claims laws, including the FCA, which can be enforced through civil " qui tam " or " whistleblower " actions, and civil monetary penalty laws, impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to " cause " the submission of false or fraudulent claims. The FCA also permits a private individual acting as a " whistleblower " to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs. Under the FCA, a " claim " also includes any request (including grant request) or demand for money or property made to the United States or to a contractor, recipient, if the Federal government provides or will reimburse any portion of the funds claimed. " Funds " include money that the NIH awards as part of research grants. Even if a federal grant is not awarded, the grant applicant may be subject to FCA liability if the information contained in or submitted as part of a grant application, including its certifications and assurances, is found to be false, fictitious, or fraudulent. • ~~the federal Health Insurance Portability and Accountability Act of 1996, or~~ HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e. g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti- Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it. • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. • the federal Physician Payments Sunshine Act, created under the ACA and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician healthcare professionals (such as physician assistants and nurse practitioners, among others), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers. • analogous state and foreign laws and regulations, such as state and foreign anti- kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third- party payor, including commercial 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 federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales

representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities, including our advisory board arrangements with physicians, some of whom receive stock or stock options as compensation for services provided, and any sales and marketing activities after a ~~product~~ **drug** candidate has been approved for marketing in the United States, could be subject to legal challenge and enforcement actions. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal, and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. In addition to the risks relating to the outcome of the independent special committee' s investigation noted above, we are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. We are subject to certain U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations. Among other matters, U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of trade laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We also expect our non- U. S. activities to increase in time. We plan to engage third parties for clinical trials or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. Risks Relating to Our Reliance on Third Parties We rely on third parties to conduct our nonclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our ~~product~~ **drug** candidates. We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, and strategic partners to conduct and support our nonclinical

studies and clinical trials under agreements with us. We expect to have to negotiate budgets and contracts with CROs, clinical trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our nonclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these nonclinical studies and clinical trials and the management of data developed through nonclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for ~~product~~ **drug** candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, 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. **In particular, protocol deviations or non- compliance with GCP requirements, or other data integrity reasons, can cause us or the FDA or other regulatory authorities to exclude data from non- compliant sites or investigators, which may cause the trial to be underpowered to meet the endpoints.** We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with pharmaceutical **drug** product produced under cGMP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. Any third parties conducting our clinical trials are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing, clinical and non- clinical ~~product~~ **drug** candidates. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our ~~product~~ **drug** candidates. As a result, our financial results and the commercial prospects for our ~~product~~ **drug** candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed. Switching or adding third parties to conduct our nonclinical studies and clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. We contract with third parties for the manufacture of our ~~product~~ **drug** candidates for nonclinical studies and our clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our ~~product~~ **drug** candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not currently have the infrastructure or internal capability to manufacture supplies of our ~~product~~ **drug** candidates for use in development and commercialization. We rely, and expect to continue to rely, on third- party manufacturers for the production of our ~~product~~ **drug** candidates for nonclinical studies and clinical trials under the guidance of members of our organization. We do not have long- term supply agreements. Furthermore, the raw materials for our ~~product~~ **drug** candidates are sourced, in some cases, from a single- source supplier and sometimes involve long lead times from order to receipt of the materials. If we were to experience an unexpected loss of supply of any of our ~~product~~ **drug** candidates or any of our future ~~product~~ **drug** 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 expect to continue to rely on third- party manufacturers for the commercial supply of any of our ~~product~~ **drug** candidates for which we obtain marketing approval. We may be unable to maintain or establish required 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 failure of the third party to manufacture our ~~product~~ **drug** candidates according to our schedule, or at all, including if our third- party contractors give greater priority to the supply of other products over our ~~product~~ **drug** candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them ; • the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms ; • the termination or nonrenewal of arrangements or agreements by our third- party contractors at a time that is costly or inconvenient for us ; • the breach by the third- party contractors of our agreements with them; • the failure of third- party contractors to comply with applicable regulatory requirements ; • the failure of the third party to manufacture our ~~product~~ **drug** candidates according to our specifications ; • the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified ; • clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales ; and • the misappropriation of our proprietary information, including our trade secrets and know- how. 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 regulations for manufacturing both active drug substances and finished drug products. Third- party

manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our ~~product~~ **drug** candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our ~~product~~ **drug** candidates, if approved. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of ~~product~~ **drug** candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our ~~product~~ **drug** candidates or drugs and harm our business and results of operations. Our current and anticipated future dependence upon others for the manufacture of our ~~product~~ **drug** candidates or drugs may adversely affect our future profit margins and our ability to commercialize any ~~product~~ **drug** candidates that receive marketing approval on a timely and competitive basis. Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals. In order to commercially produce our **drug** products either at our own facility or at a third party' s facility, we will need to comply with the FDA' s cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill- finish, packaging, or storage of our precision medicines as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our ~~product~~ **drug** candidates, including leading to significant delays in the availability of our precision medicines for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our ~~product~~ **drug** candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our ~~product~~ **drug** candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business. If our third- party manufacturers use hazardous materials in a manner that causes injury or violates applicable law, we may be liable for damages. Our research and development activities involve the controlled use of potentially hazardous substances, including chemical materials, by our third- party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations. We may use strategic collaborations, licensing arrangements or partnerships to accelerate the development and maximize the commercial potential of our programs, and we may not realize the benefits of such collaborations, arrangements or partnerships. We own worldwide rights to fosgonimeton as well as our pipeline of small molecule candidates. Where appropriate, we may use strategic collaborations, licensing arrangements or partnerships to accelerate the development and maximize the commercial potential of our programs. Any of these relationships may require us to incur non- recurring and other charges, increase our near and long- term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. We face significant competition in seeking appropriate strategic partners and the negotiation process is time- consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our ~~product~~ **drug** candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our ~~product~~ **drug** candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval. In addition, the effects to our business and reputation discussed in " — An independent special committee of our board of directors engaged in a review of papers co-authored by our former chief executive officer in connection with her doctoral research at **WSU** ~~Washington State University~~ . The special committee' s findings included that (1) our former chief executive officer altered images in her 2011 doctoral dissertation and at least four research papers that she co- authored while a graduate student at **WSU** ~~Washington State University~~ , and published from 2011 to 2014, (2) that we cited challenged research papers in certain communications and applications, and (3) that WSU' s dihexa patent, exclusively licensed to us, incorporated certain of these altered images. **WSU** ~~Washington State University~~ has undertaken a review of claims of potential research misconduct involving our former chief executive officer' s doctoral research at **WSU** ~~Washington State University~~ . We cannot predict when WSU' s investigation will be completed or what conclusions WSU will reach, " may discourage potential counterparties from entering into relationships with us. If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a ~~product~~ **drug** candidate,

reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our ~~product~~ **drug** candidates or bring them to market and generate product revenue. Even if we are successful in entering into collaborations involving our ~~product~~ **drug** candidates, these relationships are subject to numerous risks, which may include the following: • collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration; • collaborators may not pursue development and commercialization of our ~~product~~ **drug** candidates or may elect not to continue or renew development or commercialization of our ~~product~~ **drug** candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a ~~product~~ **drug** candidate, repeat or conduct new clinical trials or require a new formulation of a ~~product~~ **drug** candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our ~~product~~ **drug** candidates; • a collaborator with marketing and distribution rights to one or more **drug** products may not commit sufficient resources to their marketing and distribution; • collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability; • disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our ~~product~~ **drug** candidates, or that result in costly litigation or arbitration that diverts management attention and resources; • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable ~~product~~ **drug** candidates; and • collaborators may own or co- own intellectual property covering our **drug** products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property. As a result, if we enter into additional strategic collaborations, licensing arrangements or partnerships, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic collaboration, licensing arrangement or partnership, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new strategic collaborations, licensing arrangements or partnerships related to our ~~product~~ **drug** candidates could delay the development and commercialization of our ~~product~~ **drug** candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations. If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks. From time to time, we evaluate various acquisition opportunities and strategic transactions and partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including: • increased operating expenses and cash requirements; • the assumption of additional indebtedness or contingent liabilities; • the issuance of our equity securities; • assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel; • the diversion of our management' s attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition; • retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships; • risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and • our inability to generate revenue from acquired technology or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs. In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one- time expenses and acquire intangible assets that could result in significant future amortization expense. Risks Relating to Our Ability to Commercialize our **Drug** Product Even if approved, our ~~product~~ **drug** candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success. Even if our ~~product~~ **drug** candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance or reimbursement of any of our approved ~~product~~ **drug** candidates will depend on a number of factors, including: • the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments ; • the timing of market introduction of the ~~product~~ **drug** candidate as well as competitive products ; • the clinical indications for which the ~~product~~ **drug** candidate is approved ; • the extent of physician acceptance of FDA- approved therapies for AD or other target indications; • restrictions on the use of our ~~product~~ **drug** candidates, such as boxed warnings or contraindications in labeling, or a REMS, if any, which may not be required of alternative treatments and competitor products ; • the potential and perceived advantages of ~~product~~ **our drug** candidates over alternative treatments ; • the cost of treatment in relation to alternative treatments ; • pricing and the availability of coverage and adequate reimbursement by third- party payors, including government authorities ; • the availability of the approved ~~product~~ **drug** candidate for use as a combination therapy ; • relative convenience and ease of administration ; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies ; • the effectiveness of sales and marketing efforts ; • unfavorable publicity relating to our **drug** products or ~~product~~ **drug** candidates or similar approved products or product candidates in development by third parties ; and • the approval of other new therapies for the same indications. If any of our ~~product~~ **drug** candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or

derive sufficient revenue from such ~~product~~ **drug** candidates and our financial results could be negatively impacted. We have never commercialized a ~~product~~ **drug** candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any **drug** products on our own or together with suitable collaborators. We have never commercialized a ~~product~~ **drug** candidate. We may license certain rights with respect to our ~~product~~ **drug** candidates to collaborators, and, if so, we will rely on the assistance and guidance of those collaborators. For ~~product~~ **drug** candidates for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party. Factors that may affect our ability to commercialize our ~~product~~ **drug** candidates, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our approved ~~product~~ **drug** candidates, ensuring regulatory compliance of our company, employees and third parties under applicable healthcare laws, and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time- consuming and could delay the launch of our ~~product~~ **drug** candidates upon approval. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our ~~product~~ **drug** candidates, we may not generate revenues from them or be able to reach or sustain profitability. If the market opportunity for any ~~product~~ **drug** candidate that we develop is smaller than we believe, our revenue may be adversely affected and our business may suffer. We intend to initially focus our ~~product~~ **drug** candidate development on treatments for various CNS and ~~peripheral~~ **PNS** disorder indications. The addressable patient populations that may benefit from treatment with our ~~product~~ **drug** candidates, if approved, are based on our estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these CNS and ~~peripheral~~ **PNS** disorders. Any regulatory approval of our ~~product~~ **drug** candidates would be limited to the therapeutic indications examined in our clinical trials and as determined by the FDA, which would not permit us to market our **drug** products for any other therapeutic indications not expressly approved by the FDA. Additionally, the potentially addressable patient population for our ~~product~~ **drug** candidates may not ultimately be amenable to treatment with our ~~product~~ **drug** candidates. For example, pre- specified subgroup analysis based on topline data from our ACT-AD clinical trial identified a potential diminished effect of the combination of standard- of- care (AChEIs) and fosgonimeton. If such hypothesis is supported by additional research, patients receiving AChEIs could be excluded from the addressable patient population for fosgonimeton. Even if we receive regulatory approval for any of our ~~product~~ **drug** candidates, such approval could be conditioned upon label restrictions that materially limit the addressable patient population. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates prove to be inaccurate, the market opportunity for any ~~product~~ **drug** candidate that we or our strategic partners develop could be significantly diminished and have an adverse material impact on our business. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our ~~product~~ **drug** candidates. We face an inherent risk of product liability as a result of the planned clinical testing of our ~~product~~ **drug** candidates and will face an even greater risk if we commercialize any **drug** products. For example, we may be sued if our ~~product~~ **drug** candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our ~~product~~ **drug** candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for our ~~product~~ **drug** candidates or **drug** products that we may develop; • injury to our reputation; • withdrawal of clinical trial participants; • initiation of investigations by regulators; • costs to defend the related litigation; • diversion of management' s time and our resources; • substantial monetary awards to clinical trial participants or patients; • **drug** product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • exhaustion of any available insurance and our capital resources; • the inability to commercialize any ~~product~~ **drug** candidate; and • a decline in our share price. Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of **drug** products we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. The insurance coverage and reimbursement status of newly- approved products is uncertain. Our ~~product~~ **drug** candidates may become subject to unfavorable pricing regulations, third- party coverage and reimbursement practices, or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain adequate coverage and reimbursement for new or current **drug** products could limit our ability to market those **drug** products and decrease our ability to generate revenue. The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a **drug** product in a particular country, but then be subject to price regulations that delay

our commercial launch of the **drug** product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the **drug** product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more ~~product~~ **drug** candidates, even if any ~~product~~ **drug** candidates we may develop obtain marketing approval. In the United States and markets in other countries, patients generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our ~~product~~ **drug** candidates will depend in part on the extent to which coverage and adequate reimbursement for these **drug** products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy products. Sales of these or other future ~~product~~ **drug** candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our ~~product~~ **drug** candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third- party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our ~~product~~ **drug** candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Reimbursement by a third- party payor may depend upon a number of factors, including, but not limited to, 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. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, 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~~ **drug** candidates. Accordingly, in markets outside the United States, the reimbursement for products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for products exists among third- party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our **drug** products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours. Reimbursement agencies in Europe may be more conservative than CMS. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government- funded and private payors for any approved **drug** products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize ~~product~~ **drug** candidates, and our overall financial condition. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third- party payors for any approved **drug** products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize **drug** products and our overall financial condition. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any ~~product~~ **drug** candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any ~~product~~ **drug** candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our **drug** products compared to standard of care drugs, including lower- priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of our ~~product~~ **drug** 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 surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. A variety of risks associated with marketing our ~~product~~ **drug** candidates internationally may materially adversely affect our business. We plan to eventually seek regulatory approval of our ~~product~~ **drug** candidates outside of the United States and, accordingly, we expect that we will be

subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including: • differing regulatory requirements in foreign countries, such as the lack of pathways for accelerated drug approval, may result in foreign regulatory approvals taking longer and being more costly than obtaining approval in the United States; • foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials or our interpretation of data from nonclinical studies or clinical trials; • approval policies or regulations of foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval; • impact of ~~the~~ **health epidemics, including** COVID- 19 **,** ~~pandemic or other health epidemic~~ on our ability to produce our ~~product~~ **drug** candidates and conduct clinical trials in foreign countries; • unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements; • economic weakness, including inflation, or political instability in particular foreign economies and markets; • compliance with legal requirements applicable to privacy, data protection, information security and other matters; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • foreign taxes, including withholding of payroll taxes; • foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; • difficulties staffing and managing foreign operations; • complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries; • workforce uncertainty in countries where labor unrest is more common than in the United States; • potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations; • challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from geo- political actions, including war and terrorism. These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations. Risks Relating to Our Intellectual Property Our success depends on our ability to protect our intellectual property and our proprietary technologies. Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our ~~product~~ **drug** candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our ~~product~~ **drug** candidates, proprietary technologies and their uses that are important to our business. We may also seek to protect our proprietary position by acquiring or in- licensing relevant issued patents or pending applications from third parties. Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or the patent applications of any current or future licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around, found unenforceable or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties or the patent owner before various patent offices or in courts. Thus, the degree of future protection for our and any current or future licensors' proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties or limitations in our ability to properly protect the intellectual property rights relating to our ~~product~~ **drug** candidates could have a material adverse effect on our financial condition and results of operations. **We cannot be certain that** ~~As of December 31, 2022, our patent portfolio includes one issued U. S. patent, twelve pending U. S. patent applications, three~~ -- **the claims** ~~issued patents~~ in **our** ~~jurisdictions outside of the U. S. (not including European country validations), ten~~ pending patent applications ~~in jurisdictions outside of the U. S., and four pending international patent applications filed under the Patent Cooperation Treaty. Our owned patents and patent applications have claims directed to fosgonimeton and our other small molecule therapeutic candidates, including ATH- 1020 and ATH- 1105, as compositions of matter and methods of use thereof. The U. S. patent will expire in June 2037, absent any patent term extensions for regulatory delay. Dr. Kawas is an inventor on our company- owned patents. Our patent portfolio also includes eight issued U. S. patents and nine patents issued in jurisdictions outside of the United States (not including European country validations) that are exclusively licensed to us by WSU. The in- licensed patent portfolio includes issued U. S. patents that do not directly cover fosgonimeton as a composition of matter or pharmaceutical formulation, but instead cover the active metabolite of fosgonimeton, which is hexanoic- tyrosine- isoleucine- (6)- amino- hexanoic amide, or dihexa, and uses of dihexa. Dr. Kawas is an inventor on five of the in- licensed issued U. S. patents. We cannot be certain that the claims in our pending patent applications~~ or those of any current or future licensors ~~,~~ will be considered patentable by the ~~United States Patent and Trademark Office, or~~ USPTO ~~,~~ courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our owned or in- licensed patents will not be found invalid or unenforceable if challenged. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our ~~product~~ **drug** candidates by obtaining and defending patents. These risks and uncertainties include the following: • the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction; • patent applications may not result in any patents being issued; • patents and patent applications may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage; • changes to patent laws in the United States or in other countries may limit the ability to obtain, defend or enforce patents, or may apply retroactively to affect the terms or scope of patents; • our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our

potential ~~product~~ **drug** candidates; • there may be significant pressure on the U. S. government and international governmental bodies to limit the scope or term of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and • countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates. The patent prosecution process is also expensive and time-consuming, and we and any current or future licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or any current or future licensors will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. In addition, although we enter into non- disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third- party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed **. Certain of these parties may also be subject to public information disclosure statutes and could determine to disclose patentable aspects of our research and development output pursuant to a request thereunder** , ~~thereby~~ **notwithstanding the existence of a non- disclosure and confidentiality agreement. Any of these actions could** ~~jcopardizing~~ **jeopardize** our ability to seek patent protection. Given the amount of time required for the development, testing and regulatory review of new ~~product~~ **drug** candidates, patents protecting such candidates or their use might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of any current or future licensors may not result in patents being issued which protect our ~~product~~ **drug** candidates or their use or which effectively prevent others from commercializing competitive product candidates. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own or in- license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in- license may be challenged or circumvented by third parties or may be narrowed, invalidated or rendered unenforceable as a result of challenges by third parties. Consequently, we do not know whether our ~~product~~ **drug** candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents or the patents of any current or future licensors by developing similar or alternative technologies or products in a non- infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents or the patents of any current or future licensors may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third- party pre- issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post- grant review, or PGR, and inter partes review, or IPR, or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our ~~product~~ **drug** candidates 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. Moreover, our patents or the patents of any current or future licensors may become subject to post- grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our claim of priority of invention, scope, validity or patentability with respect to our patents and patent applications and those of any current or future licensors. For example, in view of the lawsuits disclosed elsewhere in this report including in this " Risk Factors " section under the heading " — We and certain of our directors and executive officers have been, and may in the future be, named as defendants in lawsuits that could result in substantial costs and divert management' s attention, " and in " Part I, Item 3 — Legal Proceedings, " third parties may challenge the validity or enforceability of our in- licensed patents and patent applications. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar technology and **drug** products such as other modifications to dihexa not covered by our issued patents. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our in- licensed patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop, or commercialize current or future ~~product~~ **drug** candidates. Further, these proceedings could have a material adverse effect on our business, results of operations and financial condition. Even though we own patents and patent applications covering fosgonimeton and its use, our patents and any future patents we obtain may not effectively prevent others from developing or commercializing products similar to our ~~product~~ **drug** candidates. While the fosgonimeton patent family is distinct from, and not part of the same patent family as, the dihexa patent licensed from WSU, and therefore is not implicated in the allegations that Dr. Kawas altered images in connection with her doctoral studies, third parties may use these allegations to cast doubt on the validity and enforceability of our owned patents or patent applications. Such events may result in substantial cost and require significant time from our scientists and management, and could dissuade companies from collaborating with us to license, develop, or commercialize current or future ~~product~~ **drug** candidates, even if the eventual

outcome is favorable to us. We or WSU may in the future file one or more requests for supplemental examination of certain patents for the USPTO to reconsider the enforceability and validity of the patents (including any patents relating to dihexa) in view of the allegations that Dr. Kawas altered images in connection with her doctoral studies. The outcome of any supplemental examination procedure is unpredictable. If a substantial new question of patentability is found, the USPTO Director will order ex parte reexamination of the patent. An adverse determination in such a proceeding could reduce the scope of, or invalidate or render unenforceable, the affected patent rights. While supplemental examination proceedings that result in our favor would bolster the presumption of validity and enforceability of the examined patents, third parties may still challenge the patents and patent applications in litigation or other legal proceedings. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to develop products that are similar to our ~~product~~ **drug** candidates but that are not covered by the claims of the patents that we own or license; • we or any current or future licensors or collaborators might not have been the first to make the inventions covered by the issued patents or patent application that we own or license; • we or any current or future licensors or collaborators might not have been the first to file patent applications covering certain of our or their inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that the pending patent applications we own or license will not lead to issued patents; • issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • the patents of others may have an adverse effect on our business; and • we may choose not to file a patent **application** in order to maintain certain trade secrets or know- how, and a third party may subsequently file a patent **application** covering such intellectual property. Should any of these events occur, it could significantly harm our business, results of operations and prospects. Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our ~~product~~ **drug** candidates and **drug** products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation and other legal actions, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, reexaminations, IPR proceedings and PGR proceedings and oppositions before the USPTO and / or corresponding foreign patent offices. Numerous third- party U. S. and foreign issued patents and pending patent applications exist in the fields in which we are developing ~~product~~ **drug** candidates. There may be third- party patents or patent applications with claims to compositions, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our ~~product~~ **drug** candidates. As the biopharmaceutical industry expands and more patents are issued, the risk increases that our ~~product~~ **drug** candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third- party patents or patent applications that may be infringed by commercialization of any of our ~~product~~ **drug** candidates, and we cannot be certain that we were the first to file a patent application related to a ~~product~~ **drug** candidate, its use, or our technology. Moreover, because patent applications can take many years to issue, there may be currently- pending patent applications that may later result in issued patents that our ~~product~~ **drug** candidates or their use may infringe. In addition, identification of third- party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our ~~product~~ **drug** candidates that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Any defense to claims of patent infringement asserted by third parties would be time consuming and could: • result in costly litigation that may cause negative publicity; • divert the time and attention of our technical personnel and management; • cause development delays; • prevent us from commercializing any of our ~~product~~ **drug** candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law; • require us to develop non- infringing technology, which may not be possible on a cost- effective basis; • subject us to significant liability to third parties; or • require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non- exclusive, which could result in our competitors gaining access to the same technology. Although no third party has asserted a claim of patent infringement against us as of the date of this report, others may hold proprietary rights that could prevent our ~~product~~ **drug** candidates from being marketed. Any patent- related legal action against us claiming damages and seeking to enjoin commercial activities relating to our ~~product~~ **drug** candidates, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our ~~product~~ **drug** candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion for management and other personnel. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable

terms, if at all. Moreover, even if we or a future strategic partner were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our ~~product~~ **drug** candidates, our treatment indications, or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our ~~product~~ **drug** candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our ~~product~~ **drug** candidates and technology. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. We may not be successful in obtaining or maintaining necessary rights to our ~~product~~ **drug** candidates through acquisitions and in- licenses. Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in- license, or use these third- party proprietary rights. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify as necessary for our ~~product~~ **drug** candidates. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third- party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third- party intellectual property, or if we are unable to maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or ~~product~~ **drug** candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. We may be involved in lawsuits to protect or enforce our patents or any current or future licensors' patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents or any current or future licensors' patents could be found invalid or unenforceable if challenged in court. Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable, or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our ~~product~~ **drug** candidates or their method of use, the defendant could counterclaim that our patent or the patent of any current or future licensors is invalid or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including allegations of a lack of novelty, obviousness, lack of sufficient written description, non- enablement, or obviousness-type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent application misrepresented or fraudulently withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re- examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents or any current or future licensors' patents in such a way that they no longer cover our technology or platform, or any ~~product~~ **drug** candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to a validity claim, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a third party 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 technology or platform, or any ~~product~~ **drug** candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects. The outcome following legal assertions of invalidity or unenforceability is unpredictable, and prior art could render our patents or any current or future licensors' patents invalid. There is no assurance that all potentially relevant prior art relating to our patents and patents applications or the patents and patent applications of any current or future licensors has been found. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications or the patents and patent applications of any current or future licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. Additionally, a finding that issued claims lack sufficient written description or are not enabled could render our patent or any current or future licensors' patent invalid. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we may lose at least part, and perhaps all, of the patent protection on such ~~product~~ **drug** candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of any current or future licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future ~~product~~ **drug** candidates. Such a loss of patent protection would have a material adverse impact on our business. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our management and other personnel from their normal responsibilities. In addition, there could be public announcements of the

results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented **drug** product and practicing our own patented technology. Intellectual property litigation or legal proceedings may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline. During the course of any intellectual property litigation or legal proceeding, there could be public announcements of the initiation of the litigation or legal proceeding as well as results of hearings, rulings on motions, and other interim proceedings. If securities analysts or investors regard these announcements as negative, the perceived value of our existing ~~product~~ **drug** candidates, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future **drug** products, which could have a material adverse effect on our business. Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party. Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of any current or future licensors or of third parties. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other personnel. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our ~~product~~ **drug** candidates to market. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of any current or future licensors and the enforcement or defense of our issued patents or those of any current or future licensors. On September 16, 2011, the Leahy- Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. In particular, under the Leahy- Smith Act, the United States transitioned in March 2013 to a " first inventor to file " system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that filed a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours or our current or future licensors even if we or our current or future licensors had made the invention before it was made by such third party. This requires us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or any current or future licensors are the first to either (1) file any patent application related to our ~~product~~ **drug** candidates, their use, or our technology or (2) invent any of the inventions claimed in the patents or patent applications. The Leahy- Smith Act also included a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third- party submission of printed publications to the USPTO during patent prosecution and additional procedures to attack the validity or enforceability of a patent by USPTO- administered post- grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States 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 or those of our current or future licensors that would not have been invalidated if first challenged by the third party in a district court action. Thus, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of any current or future licensors and the enforcement or defense of our issued patents or those of any current or future licensors, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Changes in U. S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our ~~product~~ **drug** candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing

biopharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third- party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. For example, 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. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the U. S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patent and the patents we might obtain or license in the future. As an example, European patent applications **now provide** ~~will soon have~~ the option, upon grant of a patent, of becoming a Unitary Patent, which **is** ~~will be~~ subject to the jurisdiction of the Unitary Patent Court, or UPC. The option of a Unitary Patent **is** ~~will be~~ a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation in the UPC. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. Patent terms may be inadequate to protect our competitive position on our ~~product~~ **drug** candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our ~~product~~ **drug** candidates or their use are obtained, once the patent life has expired, we may be open to competition from competitive products, including generic versions of our **drug** products. Given the amount of time required for the development, testing and regulatory review of new ~~product~~ **drug** candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing **drug** products similar or identical to ours. If we do not obtain patent term extension for our ~~product~~ **drug** candidates, our business may be materially harmed. Depending upon the timing, duration and specifics of FDA marketing approval of our ~~product~~ **drug** candidates, one or more of our U. S. patents or those of any current or future licensors may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during clinical trials and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our ~~product~~ **drug** candidates, although the requirements and terms of such extensions vary country- by- country. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products or launch generic versions of our **drug** products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and clinical trials by referencing our clinical and nonclinical data and launch their **drug** product earlier than might otherwise be the case. We will not be able to protect our intellectual property rights throughout the world. We own and in-license patents and pending patent applications in the United States and in jurisdictions outside of the United States. However, filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we will not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing **drug** products made using our inventions in and into the United States or other jurisdictions. Competitors may use our inventions in jurisdictions where we have not obtained patent protection to develop their own **drug** products and, further, may export otherwise infringing **drug** products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These **drug** products may compete with our ~~product~~ **drug** candidates, and our patents, the patents of any current or future licensors, or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or any current or future licensors' patents or marketing of competing **drug** products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents or the patents of any current or future licensors at risk of being

invalidated or interpreted narrowly and our patent applications or the patent applications of any current or future licensors at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such ~~patent~~ **patents** . If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Geopolitical actions could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia' s invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have a predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment, and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents or applications and those of any current or future licensors. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our **drug** products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest, and it may be difficult and costly to register, maintain or protect our rights to these trademarks and trade names in jurisdictions in and outside of the United States. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition, we rely on the protection of our trade secrets, including unpatented know- how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know- how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with our employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party improperly disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized. We may be subject to claims that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of third parties. We have entered into and may

enter in the future into non- disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third- party manufacturers, consultants, advisors, potential partners, lessees of shared multi- company property and other third parties. We may become subject to litigation where a third party asserts that we or our employees inadvertently or otherwise breached the agreements and used or disclosed their trade secrets or other information proprietary to the third parties. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our ~~product~~ **drug** candidates. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees. Parties making claims against us may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, operating results, financial condition and prospects. We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers. As is common in the biopharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our ~~product~~ **drug** candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biopharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees. Our rights to develop and commercialize our ~~product~~ **drug** candidates may be subject, in part, to the terms and conditions of licenses granted to us by others. We have entered into license agreements with third parties and we may enter into additional license agreements in the future with others to advance our research and development or allow commercialization of ~~product~~ **drug** candidates. These and other licenses may not provide exclusive rights to use such intellectual property and other rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our ~~product~~ **drug** candidates in the future **. Further, these and other licenses may also include certain restrictions or obligations that limit our ability to engage with third parties, including potential restrictions on sublicensing or outsourcing certain activities** . In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering our ~~product~~ **drug** candidates that we license from third parties. In such an event, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If any of our current or future licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our ~~product~~ **drug** candidates that are subject of such licensed rights could be adversely affected. Our licensors and any future licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in- license. If it is later determined that third parties own the rights to our in- licensed patents, or if other third parties have ownership rights to our in- licensed patents, such third parties may be able to license such patents to our competitors, and our competitors could market **drug** products similar or identical to our ~~product~~ **drug** candidates. This could have a material adverse effect on our competitive position, business, financial ~~conditions~~ **condition** , results of operations, and prospects. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same rights licensed to us. In that event, we may be required to expend significant time and resources to redesign our ~~product~~ **drug** candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected ~~product~~ **drug** candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current manufacturing methods, ~~product~~ **drug** candidates, methods of use, or future methods or ~~product~~ **drug** candidates resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties or other forms of compensation to third parties, which could be significant. If we fail to comply with our obligations in the agreements under which we license intellectual property rights or other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. Disputes may arise between us and our current or future licensors regarding intellectual property and other rights subject to a license agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • whether and the extent to which our ~~product~~ **drug** candidates infringe on intellectual property of the licensor that is not subject to the licensing agreement; • our right to sublicense to third parties; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • our right to transfer or assign the license; • the inventorship and ownership of inventions

and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and • the priority of invention of patented technology. In addition, the agreements under which we license intellectual property or other rights from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or other rights, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property or other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected ~~product~~ **drug** candidates, which could have a material adverse effect on our business, financial ~~conditions~~ **condition**, results of operations, and prospects. In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize ~~product~~ **drug** candidates covered by these license agreements. If these in- licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, **drug** products identical to ours. This could have a material adverse effect on our competitive position, business, financial ~~conditions~~ **condition**, results of operations, and prospects. The patent protection and patent prosecution for some of our ~~product~~ **drug** candidates may be dependent on third parties. While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patent applications and patents relating to our ~~product~~ **drug** candidates and their use, there may be times when the filing and prosecution activities for patent applications and patents relating to our ~~product~~ **drug** candidates are controlled by licensors or collaboration partners. If a licensor or collaboration partner fails to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patent applications and patents covering our ~~product~~ **drug** candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those ~~product~~ **drug** candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling **drug** products similar or identical to our ~~product~~ **drug** candidates. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution. Intellectual property discovered or developed through government funded programs may be subject to federal regulations such as " march- in " rights, certain reporting requirements and a manufacturing preference for U. S.- based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non- U. S. manufacturers **, which could adversely affect our ability to successfully develop and commercialize our drug products**. We **entered an exclusive license agreement with WSU for certain licensed patents that include intellectual property that was generated through the use of U. S. government funding, and we** received a grant from the **NIA** ~~National Institute on Aging~~ of the **NIH** ~~National Institute on Health~~ to support our ACT- AD clinical trial. Pursuant to the Bayh- Dole Act ~~of 1980, or the Bayh- Dole Act~~, the U. S. government may have certain rights in any invention developed or reduced to practice with ~~this~~ **government** funding. In addition, in the future we may discover, develop, acquire, or license **new** intellectual property that has been generated through the use of U. S. government funding or grants in which the U. S. government may have certain rights pursuant to the Bayh- Dole Act. These U. S. government rights include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non- exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as " march- in rights "). Such " march- in " rights would apply to new subject matter arising from the use of such government funding or grants and would not extend to pre- existing subject matter or subject matter arising from funds unrelated to the government funding or grants. If the U. S. government exercises its march- in rights in our intellectual property rights that are generated through the use of U. S. government funding or grants, we could be required to license or sublicense intellectual property discovered or developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U. S. government for the exercise of such rights. The U. S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. Reporting of a subject invention and compliance with the Bayh- Dole **Act** requirements were delayed for the patent family directed to methods of treating **AD** ~~Alzheimer' s disease~~ with fosgonimeton. As such, this patent family may be subject to U. S. government action which may include loss of rights in the subject invention, suspending or terminating the grant or future awards, or withholding further awards. Should any of these events occur, it could significantly harm our business, results of operations and prospects. In addition, the **Bayh- Dole Act** ~~U. S. government~~ requires that, in certain circumstances, any products embodying ~~any of~~ **intellectual property generated with** ~~these~~ -- **the** ~~inventions~~ **use of U. S. government funds** or produced through the use of any ~~of these inventions~~ **such intellectual property** be manufactured substantially in the United States. This preference for U. S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U. S. industry may limit our ability to contract with non- U. S. product manufacturers for products covered by such intellectual property **, which could adversely affect our ability to**

successfully develop and commercialize our drug products and have a material adverse effect on our business, financial condition, results of operations, and prospects . Risks Relating to Cybersecurity We are dependent on networks, infrastructure and data, which exposes us to data security risks, including security failures or breaches of our systems or those used by our CROs or other contractors or consultants. We are dependent upon our own or third- party information technology systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems may fail or suffer security breaches. **As discussed in this report in" Part I, Item I. C — Cybersecurity, ” we have implemented various processes and policies for identifying, assessing, and managing material risks from cybersecurity threats. However,** ~~Despite~~ **despite** the implementation of **such safeguards and** security measures, our internal computer systems and those of our CROs and other contractors and consultants may **nevertheless** be vulnerable to damage from computer viruses and unauthorized access. Likewise, data privacy or security incidents or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public or may otherwise be misused. Cyberattacks, malicious internet- based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our personal, sensitive, confidential or proprietary information and information technology systems, and those of the third parties upon which we rely **. For example, in April 2023, CRO Evotec SE faced a cybersecurity attack that temporarily disrupted its systems and operations** . Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer “ hackers, ” threat actors, “ hacktivists, ” organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation- state- supported actors. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation- state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, the third parties upon which we rely, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. We and the third parties upon which we rely may be subject to a variety of evolving threats, including but not limited to social- engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of-service attacks (such as credential stuffing), credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fires, floods, and other similar threats. Increases in remote work impacting how our employees work and access our systems could lead to additional opportunities for bad actors to launch cyberattacks or for employees to cause inadvertent security risks or incidents and may amplify the impacts of any security breach or incident. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities’ systems and technologies. We may rely on third- party service providers and technologies to operate critical business systems to process sensitive information and other company data in a variety of contexts. We may also rely on third-party service providers to provide certain products or services, or otherwise to operate our business. Our ability to monitor these third parties ~~’~~ **'** information security practices is limited, and these third parties may not have adequate information security measures in place. ~~If~~ **Security incidents or other interruptions suffered by** our third- party service providers ~~experience a security incident or other interruption, we~~ could **cause us to** experience adverse consequences. While we may be entitled to damages if our third- party service providers fail to satisfy their privacy- or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties’ infrastructure in our supply chain or our third- party partners’ supply chains have not been compromised. Our business partners face similar risks, and any security breach of, or security incident impacting, their systems or that they otherwise suffer could adversely affect our security posture. A security breach or incident or privacy violation that leads to loss of or unauthorized use, disclosure or modification of, or access to trade secrets, company resources, personal, sensitive, confidential or proprietary information, including protected health information or other patient information, or that prevents access to patient information, as well as the perception that any of the foregoing has occurred, could harm our reputation, compel us to comply with federal or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, cause us to provide other notification or take other steps in response to such breach or violation, require us to verify the correctness of database contents and otherwise subject us to litigation, claims, investigations, penalties or other liability under laws and regulations, any of which could disrupt our business or result in increased costs or loss of revenue or company resources. Moreover, the prevalent use of mobile devices that access confidential information, increase the risk of security breaches and incidents. Despite efforts to create security barriers to the above-described threats, it is impossible for us to entirely mitigate these risks. To date, we have not experienced any material impact to our business, financial position or **results of** operations resulting from cyberattacks or other information security incidents such as phishing, social engineering, ransomware or malware attacks; however, because of the frequently changing attack techniques, along with the increased volume and sophistication of such attacks, our business, financial position or **results of** operations could be adversely impacted in the future. We may be unable to anticipate or prevent techniques used to obtain unauthorized access or to compromise our systems because they change frequently and are generally not detected until after an incident has occurred. If a compromise or other security breach or incident were to occur and cause the loss or corruption of data or interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss **, unavailability, or corruption** of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Any disruption or security breach or incident resulting in ~~a~~ loss **or unavailability** of, or damage to, our data or systems, or

inappropriate use, disclosure or modification of personal, sensitive, confidential or proprietary information, could result in us incurring liability and in delays to further development and commercialization of our ~~product~~ **drug** candidates could be delayed. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or prevent or identify vulnerabilities or security breaches or incidents, that could adversely affect our business and operations or result in the loss **, unavailability, or corruption** of, or inappropriate access to or use of, critical or sensitive information or company resources. Any such interruptions, breaches or incidents, or the perception any have occurred, could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other privacy and security breaches or incidents. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims. Data collection is governed by restrictive regulations governing the use, processing and cross- border transfer of personal information. As we conduct our clinical trials and continue to enroll patients in our current and future clinical trials, we may be subject to additional restrictions relating to privacy, data protection and data security. The collection, use, storage, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals in the European Economic Area, or EEA, is subject to the EU General Data Protection Regulation, or GDPR. The GDPR is wide- ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third- party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to € 20 million or 4 % of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross- border data transfers. Certain aspects of cross- border data transfers under the GDPR are subject to uncertainty, including as the result of legal proceedings in the EU. For example, **in** ~~a July~~ 2020 **,** ~~decision by~~ the Court of Justice for the EU invalidated the EU- U. S. Privacy Shield and imposed additional obligations in connection with the use of standard contractual clauses approved by the EU Commission. These and other developments with respect to cross- border data transfers may increase the complexity of transferring personal data across borders and may require us to review and amend our mechanisms relating to cross- border data transfer. Further, the exit of the United Kingdom, or UK, from the EU has created uncertainty regarding data protection regulation in the UK. The UK has implemented legislation similar to the GDPR, referred to as the UK GDPR, which provides for fines of up to the greater of up to the greater of £ 17. 5 million or 4 % of global turnover. The GDPR and UK GDPR increased our responsibility and liability in relation to personal data that we process where subject to these regimes, and we may be required to put in place or modify policies and measures to ensure compliance with the GDPR, including as implemented by individual countries, and the UK GDPR, each of which may require us to modify our policies and procedures and engage in additional contractual negotiations, and which may cause us to incur liabilities, expenses, costs, and operational losses. Compliance with the GDPR and UK GDPR will be a rigorous and time- intensive process that may increase our cost of doing business or require us to change our business practices, and despite our efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our activities in the EEA and the UK. In addition, in the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e. g., Section 5 of the Federal Trade Commission Act), and other similar laws (e. g., wiretapping laws). California has enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt- out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The California Privacy Rights Act of 2020 (CPRA), which became operative January 1, 2023, expands the CCPA' s requirements, including applying to personal information of business representatives and employees and establishing a new regulatory agency to implement and enforce the law. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA and ~~CRPA~~ **CPRA** may increase compliance costs and potential liability with respect to other personal data we maintain about California residents. Additionally, **numerous** other states ~~, such as Virginia, Utah, Connecticut, and Colorado,~~ have proposed or enacted laws addressing privacy and security ~~that impose~~ **, including Washington' s My Health, My Data Act, and several laws imposing** obligations similar to those of the CCPA. The CCPA, CPRA, and other evolving legislation relating to privacy, data protection, and information security may impact our business activities and exemplify the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. We may also be bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the GDPR and the CCPA / CPRA, require us to impose specific contractual restrictions on our service providers, and we may also be subject to use and disclosure limitations in our contracts with providers who share information with us for clinical trials. Additionally, we may publish privacy policies, marketing materials and other statements, such as compliance with certain certifications or self- regulatory principles, regarding

data privacy and security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences. Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources. These obligations may necessitate changes to our business model, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. Compliance with U. S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Any actual or alleged failure to comply with U. S. or international laws and regulations relating to privacy, data protection, and information security could result in governmental investigations, proceedings and enforcement actions (which could result in civil or criminal penalties), private litigation or adverse publicity, harm to our reputation, and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information or impose other obligations or restrictions in connection with our use, retention and other processing of information, and we may otherwise face contractual restrictions applicable to our use, retention, and other processing of information. Claims that we have violated individuals' privacy rights, failed to comply with laws relating to privacy, data protection, or information security, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business. Risks Relating to Ownership of Our Common Stock We and certain of our directors and executive officers have been, and may in the future be, named as defendants in lawsuits that could result in substantial costs and divert management' s attention. As described elsewhere in this report in " Part I, Item 3 — Legal Proceedings, " we and certain of our executive officers and directors have been named as defendants in **a** class action ~~lawsuits~~ - **lawsuit** that generally ~~allege~~ **alleges** that we and certain of our officers and directors violated Sections 10 (b) ~~or~~ **and** 20 (a) of the Exchange Act and Rule 10b- 5 promulgated thereunder **and Sections 11, 12, and 15 of the Securities Act** by making allegedly false or misleading statements and ~~omitted~~ **omitting** material adverse facts regarding **our** ~~the Company' s~~ business **. Certain of our executive officers and directors have also been named as defendants in derivative actions, which are based on similar allegations, and generally allege that defendants breached their fiduciary duties to us, among other things. We are named as a nominal defendant in these derivative proceedings** . These complaints seek unspecified compensatory and punitive damages, and reasonable costs and expenses, including attorneys' fees **, and other relief** . As of the date of this report, we are unable to predict the outcome of these matters. Although we have insurance, it provides for a substantial retention of liability and is subject to limitations and may not cover a significant portion, or any, of the expenses or liabilities we may incur or be subject to in connection with class action lawsuit or other litigation to which we are party. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation has caused and will continue to cause our management and board of directors to divert time and attention to the litigation and could adversely impact our reputation and further divert management and our board of directors' attention and resources from other priorities, including the execution of our business plan and strategies that are important to our ability to grow our business and advance our ~~product~~ **drug** candidates, any of which could have a material adverse effect on our business. In addition, additional lawsuits may be filed, the conclusion of which in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. Actions by activist stockholders have in the past been, and may in the future be, disruptive and could cause uncertainty about the strategic direction of our business. Our business could be negatively affected as a result of stockholder activism, which could be disruptive and cause uncertainty about the strategic direction of our business. For example, in February 2022, an activist stockholder announced his intention to nominate himself and one other candidate for election to our board of directors at our 2022 annual meeting of stockholders. While this proxy contest was unsuccessful, stockholder activism could recur and have an adverse effect on our business, results of operations, and financial condition. For example, **at times** ~~as of the date of this report,~~ our market capitalization ~~was~~ **has been** less than the aggregate value of our cash, cash equivalents and investments. Other ~~similarly situated~~ biotechnology companies **in this situation** have received proposals from shareholder activists to liquidate and return capital to investors. We strive to maintain constructive communications with our stockholders and welcome their views and opinions with the goal of enhancing value for all stockholders. However, a proxy contest or other activist behaviors could have an adverse effect on us because: • responding to actions by activist stockholders can disrupt our operations, is costly and time- consuming, and diverts the attention of our board of directors and senior management team from the pursuit of business strategies, each of which could adversely affect our results of operations and financial condition; • perceived uncertainties as to our future direction as a result of changes to the composition of our board of directors may lead to the perception of a change in the direction of our business, as well as instability or lack of continuity, all of which may be exploited by our competitors, may result in the loss of potential business opportunities, may cause concern for those enrolling in our clinical trials, and make it more difficult to attract and retain qualified personnel and business partners; • actions by activist stockholders may interfere with any efforts that we undertake in the future to raise capital; • actions by activist stockholders could cause significant fluctuations in our stock price based on temporary or speculative market perceptions or other factors that do not necessarily reflect the underlying fundamentals and prospects of our business; and • if individuals are elected to our board of directors with a specific agenda as a

result of a proxy contest, it may adversely affect our ability to effectively implement our business strategy and to create additional value for our stockholders. Even if a proxy contest or other activist efforts are not successful, the increased costs that we would bear and the distraction of our board of directors and senior management could negatively impact our business, although we cannot predict with certainty the extent of such negative impacts. We do not know whether an active market for our common stock will be sustained, and, as a result, it may be difficult for you to sell your shares of our common stock. If an active market for our common stock is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our **drug** product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall. The market price of our common stock **has been and** may **continue to** be volatile, which could result in substantial losses for investors. The market price of our common stock may be volatile. As a result, you may not be able to sell your common stock at or above the price that you paid for such shares. Some of the factors that may cause the market price of our common stock to fluctuate include: • results of nonclinical studies and clinical trials; • the potential impact of ~~the~~ **health epidemics, including** COVID- 19 **,** ~~pandemic or other health epidemic~~ on our business; • the success of existing or new competitive products or technologies; • the timing and results of clinical trials for our current ~~product~~ **drug** candidates and any future ~~product~~ **drug** candidates that we may develop; • commencement or termination of collaborations for our ~~product~~ **drug** candidates; • failure or discontinuation of any of our ~~product~~ **drug** candidates; • results of nonclinical studies, clinical trials or regulatory approvals of ~~product~~ **drug** candidates of our competitors, or announcements about new research programs or ~~product~~ **drug** candidates of our competitors; • investor reactions to other companies' drug development results, including product failures or negative responses from regulatory authorities; • regulatory or legal developments in the United States and other countries; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • negative press coverage; • the status of ongoing litigation and government investigations and potential commencement of additional litigation or investigations; • the results of the investigation by the independent special committee of the board of directors and the separate ongoing investigation by WSU; • the level of expenses related to any of our research programs, ~~product~~ **drug** candidates that we may develop; • the results of our efforts to develop additional ~~product~~ **drug** candidates or **drug** products; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • announcement or expectation of additional financing efforts, including, but not limited to, under our ATM offering; • sales of our common stock by us, our insiders, or other stockholders; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in estimates or recommendations by securities analysts, if any, that cover our stock; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors **; • volatility with the banking system** ; • direct or indirect impacts on our business, our suppliers and other third parties and our clinical sites as a result of geopolitical events, including the Russia- Ukraine war; • general economic, industry, and market conditions; and • the other factors described in this " Part I, Item 1A — Risk Factors " section. In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company' s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management' s attention and resources from our business. A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well. Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. In addition, shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available- for- sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff and lock- up agreements, and Rule 144 and Rule 701 under the Securities Act ~~of 1933~~ **. Moreover** , as ~~amended, or the Securities Act. Moreover, as~~ of ~~February 28~~ **December 31** , 2023, the holders of approximately 5. ~~1~~ **7** million shares of our common stock are eligible to exercise certain rights, subject to various conditions and limitations, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also register shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline. Our directors, executive officers and significant stockholders own a substantial percentage of our common stock, which could limit your ability to affect the outcome of key transactions, including a change of control. Our directors, executive officers, significant holders of our outstanding common stock and their respective affiliates beneficially own a substantial amount of our outstanding common stock as of December 31, ~~2022~~ **2023** . As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock. We are an " emerging growth company, " and 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. For so long as we remain an emerging growth company, we are permitted and plan 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 of ~~SOX~~ **the Sarbanes- Oxley Act of 2002, or the Sarbanes- Oxley Act,** Section 404, 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. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. 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 more volatile. Failure to build **and maintain** our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies. As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes- Oxley Act ~~of 2002, or the Sarbanes- Oxley Act~~, the regulations of The Nasdaq Global Select Market, the rules and regulations of the **SEC** ~~Securities and Exchange Commission~~, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes- Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. We must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes- Oxley Act. We may experience difficulty in meeting these reporting requirements in the future. The process of building **and maintaining** our accounting and financial functions and infrastructure has required and will continue to require significant additional professional fees, internal costs and management efforts. Any disruptions or difficulties in implementing or using such a system could adversely affect our controls and harm our business. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention. In addition, we may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system' s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. If we are not able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, investors could lose confidence in our reported financial information and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Anti- takeover provisions in our charter documents and under Delaware or Washington law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and limit our stock price. Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, the amended and restated certificate of incorporation and amended and restated bylaws: • permit the board of directors to issue up to 100, 000, 000 shares of preferred stock, with any rights, preferences and privileges as they may designate; • provide that the authorized number of directors may be changed only by resolution of the board of directors; • provide that all vacancies, including newly- created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum; • divide the board of directors into three classes; • provide that a director may only be removed from the board of directors by the stockholders for cause; • require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be taken by written consent; • provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder' s notice; • prevent cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose); • provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer or by the board of directors; and • provide that stockholders are permitted to amend the bylaws only upon receiving at least two- thirds of the total votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any " interested " stockholder for a period of three years following the date on which the stockholder became an " interested " stockholder. Likewise, because our principal executive offices are located in Washington, the anti- takeover provisions of the Washington Business Corporation Act may apply to us under certain circumstances now or in the future. These provisions prohibit a " target corporation " from engaging in any of a broad range of business combinations with any stockholder constituting an " acquiring person " for a period of five years following the date on

which the stockholder became an " acquiring person. " Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States are the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware **(or, if the Court of Chancery does not have jurisdiction, another state court in Delaware or the federal district court for the District of Delaware)** will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising under the Delaware General Corporation Law, our certificate of incorporation or our amended and restated bylaws; any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or our amended and restated bylaws; and any action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U. S. federal courts have exclusive jurisdiction. Our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. The enforceability of similar exclusive federal forum provisions in other companies' organizational documents has been challenged in legal proceedings, and while the Delaware Supreme Court has ruled that this type of exclusive federal forum provision is facially valid under Delaware law, there is uncertainty as to whether other courts would enforce such provisions and that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. These exclusive forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find either exclusive forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could have a material adverse effect on our business, financial condition, and results of operations. General Risk Factors Our advisors and consultants are classified as independent contractors, and we can face consequences if it is determined that they are misclassified as such. There is often uncertainty in the application of worker classification laws, and consequently there is risk to us that our independent contractors could be deemed to be misclassified under applicable law. The tests governing whether a service provider is an independent contractor or an employee are typically highly fact sensitive and can vary by governing law. Laws and regulations that govern the status and misclassification of independent contractors are also subject to divergent interpretations by various authorities, which can create uncertainty and unpredictability. A misclassification determination or allegation creates potential exposure for us, including but not limited to monetary exposure arising from or relating to failure to withhold and remit taxes, unpaid wages, and wage and hour laws and requirements (such as those pertaining to minimum wage and overtime); claims for employee benefits, social security, workers' compensation and unemployment; claims of discrimination, harassment, and retaliation under civil rights laws; claims under laws pertaining to unionizing, collective bargaining, and other concerted activity; and other claims, charges, or other proceedings under laws and regulations applicable to employers and employees, including risks relating to allegations of joint employer liability. Such claims could result in monetary damages (including but not limited to wage- based damages or restitution, compensatory damages, liquidated damages, and punitive damages), interest, fines, penalties, costs, fees (including but not limited to attorneys' fees), criminal and other liability, assessment, or settlement. Such an allegation, claim, adverse determination, including but not limited to with respect to advisors and consultants that provide services to us could also harm our brand and reputation, which could adversely impact our business. If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. If no or few analysts commence coverage of us, the trading price of our stock could decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices. As a public company, and particularly after we are no longer an emerging growth company, we will 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. We have hired, and we expect that we will continue to need to hire, additional accounting, finance, and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time- consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We ~~are currently~~ **continue to** ~~evaluating~~ **evaluate and monitor** 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. If we are unable to maintain effective internal controls, our business, financial position and results of operations could be adversely affected. As

a public company, we are subject to reporting and other obligations under the ~~Securities~~ Exchange Act ~~of 1934~~ , **including** ~~as amended, or~~ the ~~Exchange~~ **requirements of Sarbanes- Oxley** Act ~~, including the requirements of SOX~~ Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to determine that our internal control over financial reporting is effective are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes- Oxley Act ~~of 2002~~ . These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources. Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position and results of operations. ~~Increasing attention~~ **Attention** to **ESG (** environmental, social and governance **)** matters may cause us to incur additional costs or expose us to additional risks. A variety of stakeholder groups, including investors, governmental and nongovernmental organizations are ~~increasing their focus~~ **focused** ~~and scrutiny~~ on corporate environmental, social and governance, or ESG, practices. Our ESG practices may not meet the standards of our investors or other stakeholders, and they as well as advocacy groups may campaign for us to change our business, operations or practices to better address ESG- related concerns. A failure, or perceived failure, of us to respond to any such campaigns could harm our business and reputation and have a negative impact on the market price of our common stock. Moreover, ~~as~~ **if** ESG best practices, reporting standards and disclosure requirements continue to develop, we may incur increasing costs related to ESG monitoring and reporting.