Risk Factors Comparison 2024-03-08 to 2023-03-13 Form: 10-K

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An investment in our securities involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report on Form 10- K, including our audited consolidated financial statements and related notes hereto, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects or cause our actual results to differ materially from those contained in forward- looking statements we have made in this report and those we may make from time to time. In these circumstances, the market price of our common stock could decline and you may lose all or part of your investment. We cannot assure you that any of the events discussed below will not occur. Summary of Selected Risks Associated with Our Business Our business faces significant risks and uncertainties. If any of the following risks are realized, our business, financial condition and results of operations could be materially and adversely affected. Some of the more significant risks we face include the following: • Historically, we have incurred significant operating losses and expect to continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability. • Our operating history may make it difficult to evaluate the success of our business to date and to assess our future viability. • We will require additional capital to finance our operations, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our drug development efforts or other operations. • We are early in our development efforts of our current drug candidates and all our drug candidates are in **clinical trials or** preclinical development. If we are unable to successfully develop, receive regulatory approval for and commercialize our drug candidates, or successfully develop any other drug candidates, or experience significant delays in doing so, our business will be harmed. • Our future success is dependent on the successful clinical development, regulatory approval and commercialization of our current and future drug candidates. If we, or our licensees, are not able to obtain the required regulatory approvals, we, or our licensees, will not be able to commercialize our drug candidates, and our ability to generate revenue will be adversely affected. • Because the results of preclinical studies or earlier clinical trials are not necessarily predictive of future results, our drug candidates may not have favorable results in planned or future preclinical studies or clinical trials, or may not receive regulatory approval. • Interim topline and preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures, which could result in material changes in the final data. • Preclinical studies and clinical trials are very expensive, time ~~-~~consuming and difficult to design and implement and involve uncertain outcomes. Further, we may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy in our preclinical studies and clinical trials to the satisfaction of applicable regulatory authorities. • If we are not successful in discovering, developing and commercializing additional drug candidates, our ability to expand our business and achieve our strategic objectives would be impaired. • Our drug candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval. • Even if our current or future drug candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third- party payors or others in the medical community necessary for commercial success. • Under the RLT Agreement, we are entitled to receive royalty and milestone payments in connection with the development and commercialization of soticlestat. If Takeda fails to progress, delays or discontinues the development of soticlestat, we may not receive some or all of such payments, which would materially harm our business. • Our relationships with customers, physicians, and third- party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. • Coverage and adequate reimbursement may not be available for our current or any future drug candidates, which could make it difficult for us to sell profitably, if approved. • If we are unable to obtain and maintain patent protection for our current or any future drug candidates, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets. • We may be involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time consuming and unsuccessful. • We do not have our own manufacturing capabilities and will rely on third parties to produce clinical and commercial supplies of our current and any future drug candidates. • We intend to rely on third parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business. • We may need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations. • We may be subject to numerous and varying privacy and security laws, and our failure to comply could result in penalties and reputational damage. Risks Related to Our Financial Position and Need for Additional Capital We expect to continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability. We have historically incurred significant operating losses. Our net loss was $ ~~54~~ **52** . ~~2~~ **3** million for the year ended December 31, ~~2022~~ **2023** . As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of $ ~~225~~ **277** . ~~5~~ **9** million. We expect to continue to incur increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of our drug candidates, as well as hiring employees and building our infrastructure. We have no drugs approved for commercialization and have never generated any revenue from drug sales. Most of our drug candidates are still in the preclinical testing stage. It could be several years, if ever, before we have a commercialized drug. We expect to continue to incur

significant expenses and operating losses over the next several years, and the net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if, and as, we: • continue the ongoing and planned preclinical and clinical development of our drug candidates; • continue to build a portfolio of drug candidates through the acquisition or in- license of drugs, drug candidates or technologies; • initiate preclinical studies and clinical trials for any additional drug candidates that we may pursue in the future; • seek marketing approvals for our current and future drug candidates that successfully complete clinical trials; • establish a sales, marketing and distribution infrastructure to commercialize any drug candidate for which we may obtain marketing approval; • develop, maintain, expand and protect our intellectual property portfolio; • implement operational, financial and management systems; and • attract, hire and retain additional administrative, clinical, regulatory and scientific personnel. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing our current and future drug candidates. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. Our operations have consumed substantial amounts of cash since our inception, primarily due to research and development of our drug candidates, organizing and staffing our company, business planning, raising capital, and acquiring assets. We have not yet demonstrated the ability to obtain marketing approvals, manufacture a commercial- scale drug or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had more experience developing drug candidates. We expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. We will need to eventually transition from a company with a research and development focus to a company capable of undertaking commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition. Our operations have consumed substantial amounts of cash since our inception. We expect our expenses to increase as we advance our current and future drug candidates through preclinical studies and clinical trials, commercialize our drug candidates, and pursue the acquisition or in- licensing of any additional drug candidates. Our expenses could increase beyond expectations if the FDA or other regulatory authorities require us to perform preclinical studies or clinical trials in addition to those that we currently anticipate. In addition, even if we obtain marketing approval for our drug candidates, they may not achieve commercial success. Our revenue, if any, will be derived from sales of drugs that we do not expect to be commercially available for a number of years, if at all. If we obtain marketing approval for any drug candidates that we develop or otherwise acquire, we expect to incur significant expenses related to manufacturing, marketing, sales and distribution. As of December 31, ~~2022~~ **2023**, our cash, cash equivalents and marketable securities were $ ~~129~~ **105**. ~~0~~ **8** million and we had an accumulated deficit of $ ~~225~~ **277**. ~~5~~ **9** million. We believe that our existing cash, cash equivalents and marketable securities will fund our current operating plans through at least 12 months from the filing of this Annual Report on Form 10- K. However, our operating plans may change because of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third- party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We will require more capital in order to advance the preclinical and clinical development, obtain regulatory approval and, following regulatory approval, commercialize our current or future drug candidates. Any additional capital raising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our current and future drug candidates. While the long- term economic ~~impact~~ **impacts** ~~of either~~ **associated with public health crises and geopolitical tensions, like** the **ongoing war** ~~COVID- 19 pandemic or the conflict~~ between Russia and Ukraine ~~is~~ **and war in Israel, are** difficult to assess or predict, each of these events has caused significant disruptions to the global financial markets and contributed to a general global economic slowdown. Furthermore, inflation rates have increased recently to levels not seen in decades. Increased inflation may result in increased operating costs (including labor costs) and may affect our operating budgets. In addition, the U. S. Federal Reserve has raised ~~, and is expected to further raise,~~ interest rates in response to concerns about inflation. **High** ~~Increases in~~ interest rates, especially if coupled with reduced government spending and volatility in financial markets, may further increase economic uncertainty and heighten these risks. If the disruptions and slowdown deepen or persist, we may not be able to access additional capital on favorable terms, or at all, which could in the future negatively affect our financial condition and our ability to pursue our business strategy. If we are unable to raise additional capital when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts, or grant rights to develop and market drug candidates that we would otherwise develop and market ourselves. Our ability to use our net operating loss (" NOL ") carryforwards and certain other tax attributes to offset future taxable income may be subject to limitation. Our NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities because of their limited duration or because of restrictions under U. S. tax law. Our federal NOLs generated in tax years beginning on or before December 31, 2017 are permitted to be carried forward for only 20 years under applicable U. S. tax law. Under the Tax Cuts and Jobs Act, or the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, federal NOLs incurred in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the utilization of **such** federal NOLs ~~incurred in taxable years beginning after December 31, 2020~~ is limited. In addition, under Section 382 and Section 383 of the Internal Revenue Code of 1986, as amended (**the** " Code "), and corresponding provisions of state law, if a corporation undergoes an " ownership change, " its ability to use its pre- change NOL carryforwards and other pre- change tax attributes (such as research tax credits) to offset its post- change income may be limited. A Section 382 " ownership change " generally occurs if one or more stockholders or groups of stockholders who own at least 5 % of our stock increase their ownership by more than 50 percentage points (by value) over their lowest ownership percentage over a rolling three- year period. We may have experienced ownership changes in the

past and may experience ownership changes in the future as a result of shifts in our stock ownership (some of which are outside our control). As a result, if we earn net taxable income, our ability to use our pre- change NOLs **and certain other tax attributes** to offset such taxable income may be subject to limitations. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For the years ended December 31, **2023 and** 2022 ~~and 2021~~, we recorded **no** U. S. federal ~~and~~ **or** state income tax ~~provisions~~ **provision** ~~of zero and $ 1. 3 million~~, **based** ~~respectively,~~ on pre- tax ~~loss~~ **losses** of **$ 52. 3 million and** $ 54. 2 million ~~and pre- tax income of $ 124. 2 million~~, respectively. As of December 31, ~~2022~~ **2023**, we had available approximately $ ~~153~~ **150** ~~5~~ **2** million of unused NOL carryforwards for **U. S.** federal income tax purposes, $ ~~13~~ **12** ~~0~~ **6** million of unused NOL carryforwards for Massachusetts income tax purposes, $ 164. 1 million of unused NOL carryforwards for New York income tax purposes, and $ 163. 9 million of unused NOL carryforwards for New York City income tax purposes, that may be applied against future taxable income. Our NOL carryforwards are significantly limited such that if we achieve profitability in future periods, we may not be able to utilize most of the NOL carryforwards, which could have a material adverse effect on cash flow and results of operations. Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition, or results of operations. New tax laws, statutes, rules, regulations, or ordinances could be enacted at any time. For instance, the recently enacted Inflation Reduction Act **of 2022 (the " IRA ")** imposes, among other rules, a 15 % minimum tax on the book income of certain large corporations and a 1 % excise tax on certain corporate stock repurchases. Further, existing tax laws, statutes, rules, regulations, or ordinances could be interpreted differently, changed, repealed, or modified at any time. Any such enactment, interpretation, change, repeal, or modification could adversely affect us, possibly with retroactive effect. In particular, changes in corporate tax rates, the realization of our net deferred tax assets, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act, as amended by the CARES Act or any future tax reform legislation, could have a material impact on the value of our deferred tax assets, result in significant one- time charges, and increase our future tax expenses. Risks Related to the Development and Commercialization of Our Drug Candidates We are very early in our development efforts ~~and most of our drug candidates are in preclinical development~~. If we are unable to successfully develop, receive regulatory approval for and commercialize our drug candidates ~~for these or any other indications~~, or successfully develop any other drug candidates, or experience significant delays in doing so, our business will be harmed. We are early in our development efforts ~~and most of the drug candidates for which we control developmental and commercial responsibility are still in preclinical development~~. **We** ~~For example, we~~ previously publicly announced we anticipate filing three ~~investigational new drug (" IND~~ **INDs** ") ~~applications~~ in three years, beginning in 2022 ~~,~~**;** however **,** we cannot guarantee success of preclinical development to achieve all such ~~IND~~ **INDs** ~~applications~~. Following IND acceptance, each of our drug candidates will need to be progressed through clinical development in order to achieve regulatory approval, and we will also need to address issues relating to manufacture and supply, which may involve building our own capacity and expertise. In order to commercialize any product that achieves regulatory approval, we will need to build a commercial organization or successfully outsource commercialization, all of which will require substantial investment and significant marketing efforts before we have the ability to generate any revenue from drug sales. We do not have any drugs that are approved for commercial sale, and we may never be able to develop or commercialize marketable drugs. Our ability to generate revenue from drug sales and achieve profitability depends on our ability, alone or with any current or future collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our current and future drug candidates. We do not anticipate generating revenue from drug sales for the next several years, if ever. Our ability to generate revenue from drug sales depends heavily on our, or any current or future collaborators', success in the following areas, including but not limited to: • timely and successfully completing preclinical and clinical development of our current and future drug candidates; • obtaining regulatory approvals for our current and future drug candidates for which we successfully complete clinical trials; • launching and commercializing any drug candidates for which we obtain regulatory approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner; • qualifying for coverage and adequate reimbursement by government and third- party payors for any drug candidates for which we obtain regulatory approval, both in the United States and internationally; • developing, validating and maintaining a commercially viable, sustainable, scalable, reproducible and transferable manufacturing process for our current and future drug candidates that is compliant with current good manufacturing practices (" cGMP "); • establishing and maintaining supply and manufacturing relationships with third parties that can provide an adequate amount and quality of drugs and services to support clinical development, as well as the market demand for our current and future drug candidates, if approved; • obtaining market acceptance, if and when approved, of our current or any future drug candidates as a viable treatment option by physicians, patients, third- party payors and others in the medical community; • effectively addressing any competing technological and market developments; • implementing additional internal systems and infrastructure, as needed; • negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations pursuant to such arrangements; • obtaining and maintaining orphan drug exclusivity for any of our current and future drug candidates for which we obtain regulatory approval; • maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know- how; • avoiding and defending against third- party interference or infringement claims; and • securing appropriate pricing in the United States, the European Union and other countries. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize the drug candidates we develop, which would materially harm our business. If we do not receive marketing approvals for any drug candidate we develop, we may not be able to continue our operations. We do not have any drugs that have received regulatory approval. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize our current and future drug

candidates in a timely manner. Activities associated with the development and commercialization of our current and future drug candidates are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and similar regulatory authorities outside the United States. Failure to obtain regulatory approval in the United States or other jurisdictions would prevent us from commercializing and marketing our current and future drug candidates. An inability to effectively develop and commercialize our current and future drug candidates could have an adverse effect on our business, financial condition, results of operations and growth prospects. Soticlestat, the most advanced compound we helped to develop, is continuing to be developed by Takeda and is currently in a pivotal trial program. If the pivotal trials are unsuccessful, or the compound is not approved, we will not receive the milestone payments and royalties from the RLT Agreement. Without those funds, we may need to raise significant additional capital to pursue the development and commercialization of our current and future pipeline. Further, activities associated with the development and commercialization of our current and future drug candidates are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and similar regulatory authorities outside the United States. Failure to obtain regulatory approval in the United States or other jurisdictions would prevent us from commercializing and marketing our current and future drug candidates. Even if we obtain approval from the FDA and comparable foreign regulatory authorities for our current and future drug candidates, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post- approval study or risk management requirements. If we are unable to obtain regulatory approval, or any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of that drug candidate or any other drug candidate that we may in- license, develop or acquire in the future. In certain circumstances, our third- party licensees are responsible for obtaining regulatory approvals in the countries covered by the license, and we are dependent on their efforts in order to achieve the necessary approvals in order to commercialize our products. If any future licensees fail to perform their obligations to develop and obtain regulatory approvals for the licensed products, we may not be able to commercialize our products in the affected countries, or our ability to do so may be substantially delayed. Furthermore, even if we obtain regulatory approval for our current and future drug candidates, we will still need to develop a commercial organization, establish a commercially viable pricing structure and obtain approval for adequate reimbursement from third- party and government payors. If we are unable to successfully commercialize our current and future drug candidates, we may not be able to generate sufficient revenue to continue our business. Success in preclinical testing and early clinical trials does not ensure that subsequent clinical trials will generate similar results or otherwise provide adequate data to demonstrate the efficacy and safety of a drug candidate. Frequently, drug candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. ~~For instance, our NEPTUNE trial of OV101, one of our former drug candidates, did not meet its primary endpoints despite earlier encouraging results from our Phase 2 trial STARS, the first clinical trial evaluating efficacy of OV101 in patients with Angelman syndrome. We closed our OV101 program in Angelman syndrome in early 2021.~~ The results from preclinical studies of our current and future drug candidates may not be predictive of the effects of these compounds in later stage clinical trials. If we do not observe favorable results in clinical trials of one of our drug candidates, we may decide to delay or abandon clinical development of that drug candidate. Any such delay or abandonment could harm our business, financial condition, results of operations and prospects ~~. It is difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval for our gene therapy candidates. Our future success depends in part on the successful development of our early- stage gene therapy product candidates. We may experience delays in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to internal and external commercial manufacturing sites, which may prevent us from initiating or completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all. The regulatory approval process for novel gene therapy products such as ours can be more expensive and take longer than for other product types, which are better known or more extensively studied to date. Regulatory approaches and requirements for gene therapy products continue to evolve, and any changes could create significant delay and unpredictability for product development and approval as compared to technologies with which regulatory authorities have more substantial experience. Also, before a clinical trial can begin to enroll at a site, each clinical site's Institutional Review Board (" IRB ") and its Institutional Biosafety Committee will have to review the proposed clinical trial to assess appropriateness to conduct the clinical trial at that site. In addition, adverse events in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory authorities outside the U. S. to change the requirements for human research on or for approval of any of our product candidates. Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. Trials using early versions of retroviral vectors, which integrate into, and thereby alter, the host cell' s DNA, have led to several well- publicized adverse events. The risk of serious adverse events remains a concern for gene therapy and we cannot assure that it will not occur in any of our future clinical trials. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Adverse events in trials or studies conducted by us or other parties, even if not ultimately attributable to our product candidates, and resulting publicity, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates~~ . From time to time, we have and may in the future publish or report preliminary or interim data from our clinical trials. Preliminary or interim data from our clinical trials and those of our partners

may not be indicative of the final results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and / or more patient data become available. Preliminary or topline results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published or reported. As a result, preliminary or interim data should be considered carefully and with caution until final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly. **Preclinical studies and clinical trials are very expensive, time- consuming and difficult to design and implement and involve uncertain outcomes. Further, we may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy in our preclinical studies and clinical trials to the satisfaction of applicable regulatory authorities.** All of our current drug candidates are in early clinical or preclinical development and their risk of failure is high. We must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that each of our drug candidates are safe and effective for its intended indications before we are prepared to submit **an** ~~a new drug application (“~~ NDA ~~”)~~ or ~~Biologics License Application (“~~ BLA ~~”)~~ for regulatory approval. We cannot predict with any certainty if or when we might submit an NDA or BLA for any of our product candidates or whether any such application will be approved by the FDA. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous review and regulatory requirements by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. For instance, the FDA may not agree with our proposed endpoints for any future clinical trial of our product candidates, which may delay the commencement of such clinical trial. We estimate that the successful completion of clinical trials of our product candidates will take at least several years to complete, if not longer. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Furthermore, failure can occur at any stage and we could encounter problems that cause us to abandon or repeat clinical trials. Events that may prevent successful or timely completion of clinical development include: • our inability to generate sufficient preclinical, toxicology or other data to support the initiation of clinical trials; • our inability to develop and validate disease- relevant clinical endpoints; • delays in reaching a consensus with regulatory authorities on trial design; • delays in reaching agreement on acceptable terms with prospective clinical research organizations (“ CROs ”) and clinical trial sites; • delays in opening investigational sites; • delays or difficulty in recruiting and enrollment of suitable patients to participate in our clinical trials; • imposition of a clinical hold by regulatory authorities because of a serious adverse event, concerns with a class of drug candidates or after an inspection of our clinical trial operations or trial sites; • delays in having patients complete participation in a trial or return for post- treatment follow- up; • occurrence of serious adverse events associated with the drug candidate that are viewed to outweigh its potential benefits; • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or • business interruptions resulting from **global** ~~geo- political~~ **geopolitical** ~~actions~~ **tensions** , including ~~war or the perception that hostilities may be imminent, including,~~ the ongoing war between Russia and Ukraine **and war in Israel** , **any other war or the perception that hostilities may be imminent, including** terrorism, natural disasters or public health crises. Further, clinical endpoints for certain diseases we are targeting, such as **CCM** ~~Angelman syndrome~~ , have not been established, and accordingly we may have to develop new modalities or modify existing endpoints to measure efficacy, which may increase the time it takes for us to commence or complete clinical trials. In addition, we believe investigators in this area may be inexperienced in conducting trials in this area due to the current lack of drugs to treat these disorders, which may result in increased time and expense to train investigators and open clinical sites. Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future drug sales and regulatory and commercialization milestones. In addition, if we make manufacturing or formulation changes to our drug candidates, we may need to conduct additional testing to bridge our modified drug candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our drug candidates, if approved, or allow our competitors to bring comparable drugs to market before we do, which could impair our ability to successfully commercialize our drug candidates and may harm our business, financial condition, results of operations and prospects. Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our drug candidates, we may: • be delayed in obtaining marketing approval, if at all; • 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; • be subject to additional post- marketing testing requirements; • be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; • have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy (“ REMS ”); • be subject to the addition of labeling statements, such as warnings or contraindications; • be sued; or • experience damage to our reputation. Our drug development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all. Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA’ s current ~~Good Clinical Practice (“~~ GCP ~~”)~~ regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our IND applications or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our drug candidates could be negatively impacted, and our ability to generate revenues from our drug candidates may be delayed. A key element of our current strategy is to discover, develop and potentially commercialize a portfolio of drug candidates to treat **rare** epilepsies, seizure- related disorders, and rare neurological disorders. However, our business development activities and research activities may present attractive opportunities outside of epilepsies

and seizure- related disorders and we may choose to pursue drug candidates in other areas of interest including other disorders that we believe would be in the best interest of the Company and our stockholders. We plan to continuously review our strategies and modify as necessary based on attractive areas of interest and assets that we choose to pursue. We intend to develop our portfolio of drug candidates by in- licensing and entering into collaborations with leading biopharmaceutical companies or academic institutions for new drug candidates. Identifying new drug candidates requires substantial technical, financial and human resources, whether or not any drug candidates are ultimately identified. Even if we identify drug candidates that initially show promise, we may fail to in- license or acquire these assets and may also fail to successfully develop and commercialize such drug candidates for many reasons, including the following: • the research methodology used may not be successful in identifying potential drug candidates; • competitors may develop alternatives that render any drug candidate we develop obsolete; • any drug candidate we develop may nevertheless be covered by third parties' patents or other exclusive rights; • a drug candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria; • a drug candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and • a drug candidate may not be accepted as safe and effective by physicians, patients, the medical community or third- party payors, even if approved. We have limited financial and management resources and, as a result, we may forego or delay the pursuit of opportunities with other drug candidates or for other indications that later prove to have greater market potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in circumstances under which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate. If we are unsuccessful in identifying and developing additional drug candidates or are unable to do so, our key growth strategy and business will be harmed. Enrollment and retention of patients in clinical trials is an expensive and time- consuming process and could be made more difficult or rendered impossible by multiple factors outside our control. Identifying and qualifying patients to participate in our clinical trials is critical to our success. The number of patients suffering from some of the seizure- related disorders and rare neurological disorders we are pursuing is small and has not been established with precision. If the actual number of patients with these disorders is smaller than we anticipate, we may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development and approval of our drug candidates. Even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data, the number and nature of competing treatments and ongoing clinical trials of competing therapies for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the trial, any such enrollment issues could cause delays or prevent development and approval of our drug candidates. Because we are focused on addressing seizure- related disorders and rare neurological disorders, there are limited patient pools from which to draw in order to complete our clinical trials in a timely and cost- effective manner. Furthermore, our efforts to build relationships with patient communities may not succeed, which could result in delays in patient enrollment in our clinical trials. In addition, any negative results we may report in clinical trials of our drug candidate may make it difficult or impossible to recruit and retain patients in other clinical trials of that same drug candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our drug candidates , or could render further development impossible. During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their doctor. Often, it is not possible to determine whether or not the drug candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test our drug candidates in larger, longer and more extensive clinical programs, or as use of these drug candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational drugs are tested in large- scale, Phase 3 trials or, in some cases, after they are made available to patients on a commercial scale after approval. For example, adverse events were reported in certain clinical trials for OV101, our former drug candidate, and soticlestat. Clinical trials may not demonstrate any ocular safety benefits for OV329 relative to vigabatrin. If clinical experience indicates that any of our drug candidates causes adverse events or serious or life- threatening adverse events, the development of that drug candidate may fail or be delayed, or, if the drug candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of our drug candidates, the commercial prospects of our drug candidates may be harmed and our ability to generate revenue through their sale may be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly. Additionally, if any of our drug candidates receive marketing approval, the FDA could require us to include a black box warning in our label or adopt REMS to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the drug for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by our drug candidates, several potentially significant negative consequences could result, including: • regulatory authorities may suspend or withdraw approvals of such drug candidate; • regulatory authorities may require additional warnings on the label; • we may be required to change the way a drug candidate is administered or conduct additional clinical trials; • we could be sued and held liable for harm caused to patients; • we may need to conduct a recall; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of our drug candidates and could significantly harm our business, prospects, financial condition and results of operations. If the market opportunities for our drug

candidates are smaller than we believe they are, even assuming approval of a drug candidate, our business may suffer. Because the patient populations in the market for our drug candidates may be small and difficult to assess, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth. We focus our research and drug development on treatments for **rare** epilepsies, seizure- related disorders and rare neurological disorders. Given the small number of patients who have the disorders that we are targeting, our eligible patient population and pricing estimates may differ significantly from the actual market addressable by our drug candidates. Our projections of both the number of people who have these disorders, as well as the subset of people with these disorders who have the potential to benefit from treatment with our drug candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these disorders. The number of patients may turn out to be lower than expected. Likewise, the potentially addressable patient population for each of our drug candidates may be limited or may not be amenable to treatment with our drug candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. We face substantial competition, which may result in others developing or commercializing drugs before or more successfully than us. The development and commercialization of new drugs is highly competitive. We face competition with respect to our current drug candidates and will face competition with respect to any other drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drug candidates for the treatment of the indications that we are pursuing. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. More established companies may have a competitive advantage over us due to their greater size, resources and institutional experience. In particular, these companies have greater experience and expertise in securing **collaboration or partnering relationships,** reimbursement, government contracts, relationships with key opinion leaders, conducting testing and clinical trials, obtaining and maintaining regulatory approvals and distribution relationships to market products, and marketing approved drugs. These companies also have significantly greater research and marketing capabilities than we do. If we are not able to compete effectively against existing and potential competitors, our business and financial condition may be harmed. As a result of these factors, our competitors may obtain regulatory approval of their drugs before we are able to, which may limit our ability to develop or commercialize our drug candidates. Our competitors may also develop therapies that are safer, more effective, more widely accepted and cheaper than ours, and may also be more successful than us in manufacturing and marketing their drugs. These appreciable advantages could render our drug candidates obsolete or non- competitive before we can recover the expenses of such drug candidates' development and commercialization. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Even if our current or future drug candidates receive marketing approval, they may fail to gain sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. If they do not achieve an adequate level of acceptance, we may not generate significant drug revenue and may not become profitable. The degree of market acceptance of our current or future drug candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to: • the efficacy and potential advantages compared to alternative treatments and therapies; • the safety profile of our drug candidate compared to alternative treatments and therapies; • effectiveness of sales and marketing efforts; • the strength of our relationships with patient communities; • the cost of treatment in relation to alternative treatments and therapies, including any similar generic treatments; • our ability to offer such drug for sale at competitive prices; • the convenience and ease of administration compared to alternative treatments and therapies; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the strength of marketing and distribution support; • the availability of third- party coverage and adequate reimbursement; • the prevalence and severity of any side effects; and • any restrictions on the use of the drug together with other medications. Our efforts to educate physicians, patients, third- party payors and others in the medical community on the benefits of our drug candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our drug candidates. Because we expect sales of our drug candidates, if approved, to generate substantially all of our drug revenues for the foreseeable future, the failure of our drugs to find market acceptance would harm our business and could require us to seek additional financing. Even if we obtain and maintain approval for our current or future drug candidates from the FDA, we may never obtain approval for our current or future drug candidates outside of the United States, which would limit our market opportunities and could harm our business. Approval of a drug candidate in the United States by the FDA does not ensure approval of such drug candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our current and future drug candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a drug candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the drug candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, which may require additional preclinical studies or clinical trials. In many countries outside the United States, a drug candidate must be approved

for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for any drug candidates, if approved, is also subject to approval. Obtaining approval for our current and future drug candidates in the European Union from the European Commission following the opinion of the European Medicines Agency, if we choose to submit a marketing authorization application there, would be a lengthy and expensive process. The FDA and comparable foreign regulatory authorities have the ability to limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time- consuming additional clinical trials or reporting as conditions of approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our current and future drug candidates in certain countries. In certain cases, we are dependent on third parties to obtain such foreign regulatory approvals, and any delay or failure of performance of such third parties could delay or prevent our ability to commercialize our products in the affected countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for our drug candidates may be withdrawn. If we fail to comply with the regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our current and future drug candidates will be harmed and our business, financial condition, results of operations and prospects could be harmed. If we seek approval to commercialize our current or future drug candidates outside of the United States, a variety of risks associated with international operations could harm our business. If we seek approval of our current or future drug candidates outside of the United States, we expect that we will be subject to additional risks in commercialization including: • different regulatory requirements for approval of therapies in foreign countries; • reduced protection for intellectual property rights; • the potential requirement of additional clinical studies in international jurisdictions; • unexpected changes in tariffs, trade barriers and regulatory requirements; • economic weakness, including inflation, or political instability in particular foreign economies and markets; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; • foreign reimbursement, pricing and insurance regimes; • workforce uncertainty in countries where labor unrest is more common than in the United States; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from geopolitical ~~actions~~ **tensions** , including ~~war or the perception that hostilities may be imminent (such as~~ the ongoing war between Russia and Ukraine ~~)~~ **and the war in Israel, any other war or the perception that hostilities may be imminent** , terrorism, natural disasters or public health crises. We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by many of the individual countries in and outside of Europe with which we will need to comply. Many biopharmaceutical companies have found the process of marketing their own products in foreign countries to be very challenging. Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any drug candidate that we may develop. We face an inherent risk of product liability exposure related to the testing of our current and any future drug candidates in clinical trials and may face an even greater risk if we commercialize any drug candidate that we may develop. If we cannot successfully defend ourselves against claims that any such drug candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any drug candidate that we may develop; • loss of revenue; • substantial monetary awards to trial participants or patients; • significant time and costs to defend the related litigation; • withdrawal of clinical trial participants; • the inability to commercialize any drug candidate that we may develop; and • injury to our reputation and significant negative media attention. Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any drug candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Risks Related to Licensing and Collaboration Arrangements Under the RLT Agreement, we are entitled to receive royalty and milestone payments in connection with the development and commercialization of soticlestat. If Takeda fails to progress or discontinues the development of soticlestat, we may not receive some or all of such payments, which would materially harm our business. In March 2021, we entered into the RLT Agreement, pursuant to which Takeda secured rights to our 50 % global share in soticlestat, which we had originally licensed from Takeda, and we granted to Takeda an exclusive worldwide license under our relevant intellectual property rights to develop and commercialize the investigational medicine soticlestat for the treatment of developmental and epileptic encephalopathies, including Dravet syndrome and Lennox- Gastaut syndrome. All rights in soticlestat are now owned by Takeda or exclusively licensed to Takeda by us. Following the closing date of the RLT Agreement, Takeda assumed all responsibility for, and costs of, both development and commercialization of soticlestat, and we will no longer have any financial obligation to Takeda under the original collaboration agreement, including for milestone payments or any future development and commercialization costs. Upon closing of the RLT Agreement, we received a one- time, upfront payment of $ 196. 0 million and, if soticlestat is successfully developed, we will be eligible to receive up to an additional $ 660. 0 million upon Takeda achieving specified regulatory and sales milestones. In addition, if soticlestat achieves regulatory approval, we will be entitled to receive tiered royalties at percentages ranging from the low double- digits ~~,~~ up to 20 % on sales of soticlestat. Royalties will be payable on a country- by- country and product- by- product basis during the period beginning on the date of the first commercial sale of such product in such country and ending on the later to occur of the expiration of patent rights covering the product in such country and a specified anniversary of such first commercial sale **.** **Pursuant to the Ligand Agreement, Ligand will receive a 13 % portion of the royalties and milestones owed to us pursuant to the RLT Agreement** . Under the terms of the RLT Agreement, Takeda now has sole discretion over the conduct of the development and commercialization of soticlestat. If for any reason, Takeda fails to progress, or elects to terminate the development of soticlestat as contemplated by the RLT Agreement, or if the development or commercialization of soticlestat is

delayed or deprioritized by Takeda, we may not receive some or all of the royalty and milestone payments under such agreement. We are dependent upon Takeda' s progression of such development and the resulting payments to fund the regulatory development of our current and future drug candidates. If we are unable to find alternative sources of revenue, our inability to receive royalty or milestone payments under the RLT Agreement would negatively impact our business and results of operations. Risks associated with the in- licensing or acquisition of drug candidates could cause substantial delays in the preclinical and clinical development of our drug candidates. We have previously acquired and we may acquire or in- license drug candidates for preclinical or clinical development in the future as we continue to build our pipeline. Such arrangements with third parties may impose, diligence, development and commercialization obligations, milestone payments, royalty payments, indemnification and other obligations on us. Our obligations to pay milestone, royalty and other payments to our licensors may be substantial, and the amount and timing of such payments may impact our ability to progress the development and commercialization of our drug candidates. Our rights to use any licensed intellectual property may be subject to the continuation of and our compliance with the terms of any such agreements. Additionally, disputes may arise regarding our rights to intellectual property licensed to us or acquired by us from a third party, including but not limited to: • the scope of intellectual property rights included in, and rights granted under, any license or other agreement; • the sublicensing of patent and other rights under such agreements; • our compliance with our diligence obligations under any license agreement; • the ownership of inventions and know- how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators; • the scope and duration of our payment obligations, and our ability to make such payments when they are owed; • our need to acquire additional intellectual property rights from third parties that may impact payments due under such agreements; • the rights of our licensors to terminate any such agreement; • our rights and obligations upon termination of such agreement; and • the scope and duration of exclusivity obligations of each party to the agreement. Disputes over intellectual property and other rights that we have licensed or acquired, or may license or acquire in the future, from third parties could prevent or impair our ability to maintain any such arrangements on acceptable terms, result in delays in the commencement or completion of our preclinical studies and clinical trials and impact our ability to successfully develop and commercialize the affected drug candidates. If we fail to comply with our obligations under any future licensing agreements, these agreements may be terminated or the scope of our rights under them may be reduced and we might be unable to develop, manufacture or market any product that is licensed under these agreements. We may be required to relinquish important rights to and control over the development and commercialization of our drug candidates to any future collaborators. Our current and future collaborations could subject us to a number of risks, including: • we may be required to undertake the expenditure of substantial operational, financial and management resources; • we may be required to issue equity securities that would dilute our stockholders' percentage of ownership; • we may be required to assume substantial actual or contingent liabilities; • we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our drug candidates; • strategic collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new version of a drug candidate for clinical testing; • strategic collaborators may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs; • strategic collaborators may not commit adequate resources to the marketing and distribution of our drug candidates, limiting our potential revenues from these products; • we rely on our current collaborators to manufacture drug substance and drug product and may do so with respect to future collaborators, which could result in disputes or delays; • disputes may arise between us and our strategic collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts management' s attention and consumes resources; • disputes may arise between us and our current or future collaborators regarding any termination of any collaboration, license, or other business development arrangement in which we may enter; • strategic collaborators may experience financial difficulties; • strategic collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation; • business combinations or significant changes in a strategic collaborator' s business strategy may also adversely affect a strategic collaborator' s willingness or ability to complete its obligations under any arrangement; • strategic collaborators could decide to move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and • strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our drug candidates. 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. Our business plan is to continue to evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary drugs, 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; • assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel; • the diversion of our management' s attention from our existing drug programs and initiatives in pursuing such a strategic partnership, 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 drugs or drug candidates and regulatory approvals; • our inability to generate revenue from acquired technology and / or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs; • challenges related to integrating acquired businesses or entering into or realizing the benefits of strategic transactions generally; and • risks associated with potential international acquisition transactions, including in countries where we do not currently have a material presence. In addition, if we engage in future acquisitions or strategic partnerships, 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. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or drugs that may be important to the development of our business. We may explore additional strategic collaborations that may never materialize or may fail. Our business strategy is based on acquiring or in- licensing compounds directed at **rare** epilepsies, seizure- related disorders, and rare neurological disorders. As a result, we intend to periodically explore a variety of possible additional strategic collaborations in an effort to gain access to additional drug candidates or resources. At the current time, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic collaborations because of the numerous risks and uncertainties associated with establishing them. Further, our business development activities and research activities may present attractive opportunities outside of **rare** epilepsies and seizure- related disorders and we may choose to pursue drug candidates in other areas of interest including other disorders and diseases that we believe would be in the best interest of the Company and our stockholders. We plan to continuously review our strategies and modify as necessary based on attractive areas of interest and assets that we choose to pursue. Risks Related to Regulatory Compliance Healthcare providers and third- party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third- party payors may subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct or may conduct our business. The laws that will affect our operations include, but are not limited to: • the federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the " PPACA "), amended the intent requirement of the federal Anti- Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation; • federal civil and criminal false claims laws, including, without limitation, the False Claims Act, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The PPACA provides, and recent government cases against pharmaceutical and medical device manufacturers support, the view that federal Anti- Kickback Statute violations and certain marketing practices, including off- label promotion, may implicate the False Claims Act; • the federal Health Insurance Portability and Accountability Act of 1996 (" HIPAA "), which created additional federal criminal statutes that prohibit a person from knowingly and willfully executing a scheme or making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e. g., public or private); • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (" HITECH "), and their implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, and their respective business associates, individuals or entities that perform certain services on behalf of a covered entity that involves the use or disclosure of individually identifiable health information and their subcontractors that use, disclose or otherwise process individually identifiable health information; • Physician Payments Sunshine Act, which is part of the PPACA, that require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services (" CMS "), information related to: (i) payments or other " transfers of value " made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals; and (ii) ownership and investment interests held by physicians and their immediate family members; • state and foreign law equivalents of each of the above federal laws, state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and / or information regarding drug pricing, 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 or to adopt compliance programs as prescribed by state laws and regulations, or that otherwise restrict payments that may be made to healthcare providers, state laws and regulations that require drug manufacturers to file reports relating to drug pricing and marketing information, and state and local laws that require the registration of pharmaceutical sales representatives; and • state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws and the curtailment or restructuring of our operations. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management' s attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and / or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements. Market acceptance and sales of any drug candidates that we commercialize, if approved, will depend in part on the extent to which coverage and adequate reimbursement for these drugs and related treatments will be available from third- party payors, including government health administration authorities, managed care organizations and other private health insurers. Third- party payors decide which therapies they will pay for and establish reimbursement levels. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any drug candidates that we develop will be made on a payor- by- payor basis. One third- party payor' s determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third- party payor' s decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each third- party payor determines whether or not it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a third- party payor' s list of covered drugs, or formulary, generally determines the co- payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third- party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our drugs unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our drugs. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our current and any future drug candidates that we develop. Further, coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained, less favorable coverage policies and reimbursement rates may be implemented in the future. Healthcare legislative reform measures may have a negative impact on our business and results of operations. In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of drug candidates, restrict or regulate post- approval activities, and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and / or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the PPACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U. S. pharmaceutical industry. There have been executive, judicial, Congressional and executive branch challenges to certain aspects of the PPACA. For example, **on** ~~President Trump signed Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress considered legislation to repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the PPACA such as removing penalties, effective January 1, 2019, for not complying with the PPACA' s individual mandate to carry health insurance, delaying the implementation of certain PPACA- mandated fees, and increasing the point- of- sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. On~~ June 17, 2021 the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the PPACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Further, there have been a number of health reform measures by the Biden administration that have impacted the PPACA. **On** ~~For example, on~~ August 16, 2022, President Biden signed the ~~Inflation Reduction Act of 2022 (" IRA "),~~ into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in PPACA marketplaces through plan year 2025. The IRA also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of- pocket cost and by creating a new manufacturer discount program. It is possible that the PPACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden

administration will impact the PPACA and our business. Other legislative changes have been proposed and adopted since the PPACA was enacted. These 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 due to subsequent legislative amendments to the statute, will remain in effect until ~~2031~~ **2032** unless additional Congressional action is taken ~~. Under current legislation, the actual reduction in Medicare payments will vary from 1 % in 2022 to up to 4 % in the final fiscal year of this sequester~~. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015 (“ MACRA ”), which ended the use of the statutory formula and established a quality payment program, also referred to as the Quality Payment Program. **This program provides clinicians with** ~~In November 2019, CMS issued a final rule finalizing the changes to~~ **two ways to participate, including through** the ~~Quality~~ **Advanced Alternative** Payment ~~Program. At this time,~~ **Models (“ APMs ”) and** the **Merit- based Incentive** ~~full impact to overall physician reimbursement as a result of the introduction of the Quality~~ Payment ~~Program remains unclear~~ **System (“ MIPS ”). Under both APMs and MIPS, performance data collected each performance year will affect Medicare payments in later years, including potentially reducing payments**. Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, in July 2021, the Biden administration released an executive order, “ Promoting Competition in the American Economy, ” with multiple provisions aimed at prescription drugs. In response to Biden’ s executive order, on September 9, 2021, the U. S. Department of Health and Human Services (~~"~~ **“** HHS ~~"~~ **”**) released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. Further, the IRA, among other things (i) directs HHS to negotiate the price of certain high- expenditure, single- source drugs and biologics covered under Medicare and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions ~~will~~ take effect progressively starting in fiscal year 2023 **. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations**, although ~~they~~ **the** ~~may be~~ **Medicare drug price negotiation program is currently** subject to legal challenges. Additionally, the Biden administration released an additional executive order on October 14, 2022, directing HHS to report 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. At the state level, legislatures have increasingly passed and implemented regulations designed to control pharmaceutical and biological product pricing, including pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. For example, ~~based on a recent~~ **in response to the Biden administration’ s October 2022** executive order, **on February 14, 2023, HHS released a report outlining three new models for testing by the Centers for Medicare & Medicaid Services Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023,** the Biden administration **announced an** ~~expressed its intent to pursue certain policy initiatives~~ **initiative** to ~~reduce drug~~ **control the** ~~prices~~ **price of prescription drugs through the use of march- in rights under the Bayh- Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework**. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. We may not be able to obtain or maintain orphan drug designations or exclusivity for our drug candidates, which could limit the potential profitability of our drug candidates. Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals in the United States. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for an indication for which it receives the designation, then the drug is entitled to a period of marketing exclusivity that precludes the applicable regulatory authority from approving another marketing application for the same drug for the same indication for the exclusivity period except in limited situations. For purposes of small molecule drugs, the FDA defines “ same drug ” as a drug that contains the same active moiety and is intended for the same use as the drug in question. A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Obtaining orphan drug designations is important to our business strategy; however, obtaining an orphan drug designation can be difficult and we may not be successful in doing so. Even if we were to obtain orphan drug designation for a drug candidate, we may not obtain orphan exclusivity and that exclusivity may not effectively protect the drug from the competition of different drugs for the same

condition, which could be approved during the exclusivity period. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same drug for the same indication if the FDA concludes that the later drug is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusive marketing rights in the United States also may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. The failure to obtain an orphan drug designation for any drug candidates we may develop, the inability to maintain that designation for the duration of the applicable period, or the inability to obtain or maintain orphan drug exclusivity could reduce our ability to make sufficient sales of the applicable drug candidate to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition. Even if we obtain regulatory approval for our current or future drug candidates, they will remain subject to ongoing regulatory oversight. Even if we obtain any regulatory approval for our current or future drug candidates, such approvals will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping and submission of safety and other post- market information. Any regulatory approvals that we receive for our current or future drug candidates may also be subject to a REMS, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 trials, and surveillance to monitor the quality, safety and efficacy of the drug. In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA, BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing. If we fail to comply with applicable regulatory requirements following approval of our current or future drug candidates, a regulatory authority may: • issue an untitled letter or warning letter asserting that we are in violation of the law; • seek an injunction or impose administrative, civil or criminal penalties or monetary fines; • suspend or withdraw regulatory approval; • suspend any ongoing clinical trials; • refuse to approve a pending NDA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners; • restrict the marketing or manufacturing of the drug; • seize or detain the drug or otherwise require the withdrawal of the drug from the market; • refuse to permit the import or export of drug candidates; or • refuse to allow us to enter into supply contracts, including government contracts. 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. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our current or future drug candidates and harm our business, financial condition, results of operations and prospects. In addition, the FDA' s policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could cause changes to or delays in the drug review process, or suspend or restrict regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would harm our business, financial condition, results of operations and prospects. Risks Related to Our Intellectual Property We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our development programs and drug candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our current and any future drug candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our current and future development programs and drug candidates. The patent prosecution process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own or in- license may fail to result in issued patents with claims that cover our current or any future drug candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our current or any future drug candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any drug candidates or companion diagnostic that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a drug candidate and companion diagnostic under patent protection could be reduced. If the patent applications we hold or have in- licensed with respect to our development programs and drug candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current or any future drug candidates, it could dissuade companies from collaborating with us to develop drug candidates, and threaten our ability to commercialize, future drugs. Any such outcome could have a negative effect on our business. The patent position of biotechnology and pharmaceutical

companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or drugs, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drugs. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On December 16, 2011, the Leahy-Smith America Invents Act (~~the~~ " Leahy- Smith Act ") was signed into law. The Leahy- Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent Office recently developed new regulations and procedures to govern administration of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy- Smith Act will have on the operation of our business. However, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business and financial condition. Moreover, we may be subject to a third- party pre- issuance submission of prior art to the ~~U. S. Patent and Trademark Office (" the~~ USPTO ~~")~~ or become involved in opposition, derivation, reexamination, inter partes review, post- grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third- party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our technology and drugs. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years from the earliest filing date of a non- provisional patent application. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future drug candidates, we may be open to competition from generic versions of such drugs. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and / or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned and licensed patents and / or applications and any patent rights we may own or license in the future. We rely on our outside counsel or our licensing partners to pay these fees due to non- U. S. patent agencies. The USPTO and various non- U. S. government patent agencies require compliance with several 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 we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non- compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business. Patent terms may be inadequate to protect our competitive position on our drug candidates for an adequate amount of time. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their

drug earlier than might otherwise be the case. Intellectual property rights do not necessarily address all potential threats to our business. 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. The following examples are illustrative: • others may be able to make compounds or formulations that are similar to our drug candidates but that are not covered by the claims of any patents, should they issue, that we own or control; • we or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or control; • we might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that our pending patent applications will not lead to issued patents; • issued patents that we own or control may not provide us with any competitive advantages, or may be held invalid or unenforceable because of legal challenges; • our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; and • the patents of others may have an adverse effect on our business. The proprietary map of disease- relevant biological pathways underlying orphan disorders of the brain that we developed would not be appropriate for patent protection and, as a result, we rely on trade secrets to protect this aspect of our business. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business. Our commercial success depends, in part, upon our ability and the ability of our current or future collaborators to develop, manufacture, market and sell our current and any future drug candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and any future drug candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third- party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future drug candidates. In order to successfully challenge the validity of any such U. S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U. S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U. S. patent. If we are found to infringe a third party' s valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our drug candidate (s) and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non- exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or drug candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our current or any future drug candidates or force us to cease some or all of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects. See the section herein titled " Legal Proceedings " for additional information. We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property. Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual' s current or former employer. 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. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time- consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of

being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third party may also cause the third party to bring counter claims against us such as claims asserting that our patents are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non- enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post- grant proceedings such as ex parte reexaminations, inter partes review, or post- grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future drug candidates. Such a loss of patent protection could harm our business. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock. Changes in U. S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our current and any future drug candidates. The United States has recently enacted and implemented wide- ranging patent reform legislation. 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 actions by the U. S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future. We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business. Filing, prosecuting and defending patents covering our current and any future drug candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These drugs may compete with our drugs in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. If we rely on third parties to manufacture or commercialize our current or any future drug candidates, or if we collaborate with additional third parties for the development of our current or any future drug candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third- party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations. In addition, these agreements typically restrict the ability of our advisors, employees, third- party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any third- party collaborators. A competitor' s discovery of our trade secrets would harm our business. Risks Related to Our Dependence on Third Parties We do not own or operate, and we do not expect to own or operate, facilities for drug manufacturing, drug formulation, storage and distribution ,or testing. We have been in the past, and will continue to be, dependent on third parties to manufacture the clinical supplies of our drug candidates. Further, we also will rely on third- party manufacturers to supply us with sufficient quantities of our drug candidates to be used, if approved, for commercialization. Any significant delay in the supply of a drug candidate, or the raw material components thereof, for an

ongoing clinical trial due to the need to replace a third- party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our drug candidates. Further, our reliance on third- party manufacturers entails risks to which we would not be subject if we manufactured drug candidates ourselves including: • inability to meet our drug specifications and quality requirements consistently; • delay or inability to procure or expand sufficient manufacturing capacity; • issues related to scale- up of manufacturing; • costs and validation of new equipment and facilities required for scale- up; • failure to comply with cGMP and similar foreign standards; • inability to negotiate manufacturing agreements with third parties under commercially reasonable terms, if at all; • termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; • reliance on single sources for drug components; • lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier; • operations of our third- party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and • carrier disruptions or increased costs that are beyond our control. Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our current or any future drug candidates once approved. Some of these events could be the basis for FDA action, including injunction, request for recall, seizure, or total or partial suspension of production. We do not currently have the ability to independently conduct any preclinical studies or clinical trials. We intend to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our preclinical studies and clinical trials, and we expect to have limited influence over their actual performance. We intend to rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future preclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies or clinical trials are conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs will be required to comply with good laboratory practices (" GLPs ") and GCPs, which are regulations and guidelines enforced by the FDA and are also required by the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities in the form of International Council for Harmonization guidelines for any of our drug candidates that are in preclinical and clinical development. The regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we will rely on CROs to conduct GCP- compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. If we or our CROs fail to comply with GCPs, 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. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process. While we will have agreements governing their activities, our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and preclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any drug candidate that we develop. As a result, our financial results and the commercial prospects for any drug candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA 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 and may ultimately lead to the denial of marketing approval of our current and future drug candidates. If our relationship with these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, financial condition and prospects. Risks Related to Our Business Operations, Employee Matters and Managing Growth We are highly dependent on the services of our senior management team, including our Chairman and Chief Executive Officer, Dr. Jeremy Levin, and if we are not able to retain these members of our management team or recruit and retain additional management, clinical and scientific personnel, our business will be harmed. We are highly dependent on our senior management team, including our Chairman and Chief Executive Officer, Dr. Levin. The employment agreements we have with these officers do not prevent such persons from terminating their employment with us at any time. The loss of the services of any of these persons could impede the achievement of our research, development, operational, financial and commercialization objectives. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management and to attract, on

acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. This risk may be further amplified given the particularly competitive hiring market in New York City, the location of our corporate headquarters. We may not be able to attract or retain qualified personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high- quality candidates and consultants than what we have to offer. If we are unable to continue to attract, retain and motivate high- quality personnel and consultants to accomplish our business objectives, the rate and success at which we can discover and develop drug candidates and our business will be limited and we may experience constraints on our development objectives. Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our drug candidates, harming future regulatory approvals, sales of our drug candidates and our results of operations. Additionally, we do not currently maintain " key person " life insurance on the lives of our executives or any of our employees. As of December 31, ~~2022~~ **2023**, we had ~~44~~ **40** full- time employees. As our development and commercialization plans and strategies for our current pipeline of product candidates develop, we expect to need additional managerial, operational, sales, marketing, financial, legal and other resources. Our management may need to divert a disproportionate amount of its attention away from our day- to- day operations and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational inefficiencies, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of our current and potential future drug candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance, our ability to commercialize drug candidates, develop a scalable infrastructure and compete effectively will depend, in part, on our ability to effectively manage any future growth. Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk that our employees, consultants, distributors, and collaborators may engage in fraudulent or illegal activity. Misconduct by these parties could include intentional, reckless or negligent conduct or disclosure of unauthorized activities to us that violates the regulations of the FDA and non- U. S. regulators, including those laws requiring the reporting of true, complete and accurate information to such regulators, manufacturing standards, healthcare fraud and abuse laws and regulations in the United States and abroad or laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry, including the sale of pharmaceuticals, 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. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Further, because of our hybrid- work policies, information that is normally protected, including company confidential information, may be less secure. If actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of significant fines or other sanctions, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal 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, contractual damages, reputational harm, diminished profits and future earnings and curtailment of operations, any of which could adversely affect our ability to operate our business and our results of operations. Whether or not we are successful in defending against such actions or investigations, we could incur substantial costs, including legal fees, and divert the attention of management in defending ourselves against any of these claims or investigations. Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us. We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, process and transmit large amounts of sensitive ~~information~~ **data**, ~~including intellectual property, proprietary business information, personal information~~ and **, as a result, we and** ~~other~~ -- **the** ~~confidential information. It is critical~~ **third parties upon which we rely face a variety of evolving threats** that **could cause security incidents** ~~we do so in a secure manner to maintain the confidentiality, integrity and availability of such sensitive information~~. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result, we manage a number of third- party vendors who may or could have access to our computer networks or our ~~confidential information~~ **sensitive data**. In addition, many of those third parties in turn subcontract or outsource some of their responsibilities to **other** third parties. While all information technology operations are inherently vulnerable to inadvertent or intentional security breaches, incidents, attacks and exposures, the accessibility and distributed nature of our information technology systems, and the sensitive ~~information~~ **data** stored on those systems, make such systems ~~potentially~~ vulnerable to

unintentional or malicious, internal and external attacks on our technology environment **. Furthermore, our ability to monitor the aforementioned third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third- party service providers experience a security incident or other interruption, we could 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** . In addition, due to our hybrid- work environment, we may be more vulnerable to cyberattacks **as more of our employees utilize network connections, computers, and devices outside our premises or network, including working at home, while in transit and in public locations. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program** . Potential vulnerabilities can be exploited from inadvertent or intentional actions of our employees, third- party vendors, business partners, or by malicious third parties. ~~Attacks~~ **We take steps designed to detect, mitigate, and remediate vulnerabilities in our information systems (such as our hardware and / or software, including that** of ~~this nature~~ **third parties upon which we rely); however we may not detect and remediate all such vulnerabilities on a timely basis. Further, we may experience delays in deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident. Cyberattacks, malicious internet- based activity, online and offline fraud, and other similar activities** are increasing in their frequency, levels of persistence, sophistication and intensity, and are **also** being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, " hacktivists, " nation states and others. ~~In addition to the extraction of sensitive information, such~~ **Such** attacks could include the deployment of harmful malware **(including as a result of advanced persistent threat intrusions)** , ransomware **attacks** , denial- of- service attacks, **credential stuffing and / or harvesting,** social engineering **(including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), supply- chain attacks, software bugs, server malfunctions, software or hardware failures, loss of sensitive data or other information technology assets, adware, attacks enhanced or facilitated by artificial intelligence, telecommunications failures, earthquakes, fires, floods** and other means to affect service reliability and threaten the confidentiality, integrity and availability of **our** information **systems and sensitive data** . In ~~addition~~ **particular** , ~~the~~ **severe ransomware attacks are becoming increasingly** prevalent ~~use of mobile~~ **and can lead to significant interruptions in our operations, ability to provide our products or** ~~devices~~ **services , loss** ~~increases the risk~~ of **sensitive** data ~~security incidents~~ **and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments** . Significant disruptions of our, our third- party vendors' and / or business partners' information technology systems or other similar data security incidents could adversely affect our business operations and / or result in the loss, misappropriation, and / or unauthorized access, use or disclosure of, or the prevention of access to, sensitive ~~information~~ **data** , which could result in financial, legal, regulatory, business and reputational harm to us. In addition, information technology system disruptions, whether from attacks on our technology environment or from computer viruses, natural disasters, terrorism, war and telecommunication and electrical failures, could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. ~~There is no way~~ **We may expend significant resources or modify our business activities to try to protect against security incidents. Additionally, certain data privacy and security obligations may require us to implement and maintain specific security measures or industry- standard or reasonable security measures to protect our information technology systems and sensitive data. Applicable data privacy and security obligations may require us to notify relevant stakeholders, including affected individuals, customers, regulators, and investors,** of ~~knowing~~ **security incidents. Such disclosures are costly, and the disclosure or the failure to comply** with ~~certainty whether~~ **such requirements could lead to adverse consequences. If** we **(or a third party upon whom we rely) experience a security incident or are perceived to** have experienced **a** ~~any data~~ security ~~incidents~~ **incident** ~~that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the way they conceal access to systems, and many companies that have been attacked are not aware that they have been attacked. Any event that leads to unauthorized access, use or disclosure of personal information~~ , including but not limited to **a security incident involving** personal information regarding our patients or employees, ~~could~~ **we may experience adverse consequences, such as** ~~disrupt~~ **disruptions to** our business, harm **to** our reputation, ~~compel us to comply with applicable federal~~ **government enforcement actions (for example, investigations, fines, penalties, audits, and inspections), additional reporting requirements,** and / or **oversight** ~~state breach notification laws and foreign law equivalents~~ , **or we may otherwise be** subject ~~us to time consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to verify the correctness of database contents, or otherwise subject us~~ to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us, and result in significant legal and financial exposure and / or reputational harm. In addition, any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security- related legal or other obligations to third parties, or any further security incidents or other inappropriate access events that result in the

unauthorized access, release or transfer of sensitive **data** ~~information, which could include personally identifiable information~~ , may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us or we could be subject to claims by third parties that we have breached our privacy- or confidentiality- related obligations, which could materially and adversely affect our business and prospects. Moreover, data security incidents and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will ~~successfully prevent service interruptions~~ **be effective. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in** ~~or~~ **our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and** security ~~incidents~~ **obligations** . We are subject **to stringent and evolving privacy and security laws, regulations, contractual obligations, industry standards, policies, and other obligations, and our failure or perceived failure to comply with such obligations could result in regulatory investigations or actions, litigation (including class actions), fines and penalties, disruptions of our business operations, loss of revenue or profits, reputational damage and other adverse business consequences. In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, sensitive third-party data, business plans, transactions, clinical trial data and financial information (collectively, sensitive data). Our data processing activities subject us** to laws and regulations covering data privacy and the protection of personal information ~~including health information~~ **and other sensitive data** . The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which may affect our business. In the United States, we may be subject to state security breach notification laws, state health information privacy laws and federal and state consumer protections laws which impose requirements for the collection, use, disclosure and transmission of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. If we fail to comply with applicable laws and regulations, we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA. Numerous other countries have, or are developing, laws governing the collection, use and transmission of personal information as well. EU member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations. For example, in May 2016, the EU formally adopted the General Data Protection Regulation ~~, or~~ **(“** GDPR **”)** , which applies to all EU member states as of May 25, 2018 and replaces the former EU Data Protection Directive. The regulation introduces new data protection requirements in the EU and imposes substantial fines for breaches of the data protection rules. The GDPR must be implemented into national laws by the EU member states imposes strict obligations and restrictions on the ability to collect, analyze, and transfer personal data, including health data from clinical trials and adverse event reporting. Data protection authorities from different EU member states have interpreted the privacy laws differently, which adds to the complexity of processing personal data in the EU, and guidance on implementation and compliance practices are often updated or otherwise revised. Any failure to comply with the rules arising from the GDPR and related national laws of EU member states could lead to government enforcement actions and ~~significant penalties against us~~ **fines of up to 20 million Euros or 4 % of annual global revenue, whichever is greater** , and adversely impact our operating results. The GDPR will increase our responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with EU data protection rules. Additionally, California enacted the California Consumer Privacy Act **of 2018, as amended by the California Privacy Rights Act of 2020** (the “ CCPA ”) **which** ~~legislation that~~ has been dubbed the first “ GDPR- like ” law in the United States. **In the past few years, numerous other U. S. states — including Virginia, Colorado, Connecticut, and Utah — have also enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data.** The CCPA gives California residents expanded rights to access **, correct** and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt- out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. ~~The~~ **Although there are limited exemptions for clinical trial data under the** CCPA **(and the other similar state privacy laws), the CCPA and other similar laws** may ~~increase~~ **impact (possibly significantly) our business activities depending on how it is interpreted, should we become subject to the CCPA in the future. In addition to data privacy and security laws, we may be bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We also publish privacy policies, marketing materials, and other statements regarding data privacy and security and if these policies, materials,** ~~our~~ **or** ~~compliance costs~~ **statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy** and ~~potential liability~~ **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. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement**

actions (e. g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class- action claims) and mass arbitration demands; additional reporting requirements and / or oversight; bans on processing personal data (including clinical trial data); and orders to destroy or not use personal data . Risks Related to Being a Public Company We are a " smaller reporting company " and the reduced disclosure requirements applicable to such companies may make our common stock less attractive to investors. We are currently a " smaller reporting company " as defined in the Securities Exchange Act of 1934, as amended (the " Exchange Act "). We will be a smaller reporting company and may take advantage of the scaled- back disclosures available to smaller reporting companies for so long as (i) the market value of our voting and non- voting ordinary shares held by non- affiliates is less than $ 250. 0 million measured on the last business day of our second fiscal quarter or (ii) (a) our annual revenue is less than $ 100. 0 million during the most recently completed fiscal year and (b) the market value of our voting and non- voting ordinary shares held by non- affiliates is less than $ 700. 0 million measured on the last business day of our second fiscal quarter. As a smaller reporting company, we are permitted to comply with scaled- back disclosure obligations in our SEC filings compared to other issuers, including with respect to disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We have elected to adopt the accommodations available to smaller reporting companies. Until we cease to be a smaller reporting company, the scaled- back disclosure in our SEC filings will result in less information about our company being available than for other public companies. If investors consider our common shares less attractive as a result of our election to use the scaled- back disclosure permitted for smaller reporting companies, there may be a less active trading market for our common shares and our share price may be more volatile. We may take advantage of certain of the scaled- back disclosures available to smaller reporting companies, including but not limited to: • reduced disclosure obligations regarding executive compensation arrangements; and • being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced " Management' s Discussion and Analysis of Financial Condition and Results of Operations " disclosure. ~~Effective as of December 31, 2022, we ceased to be an" emerging growth company", which will increase our costs and demands on management. On December 31, 2022, we ceased to be an emerging growth company (" EGC "), as defined in the Jumpstart Our Business Startups Act of 2012. In addition, as a result of the market value of our common stock held by non- affiliates as of June 30, 2022, we also qualified as a smaller reporting company and an accelerated filer. Due to our exit from EGC status and our qualification as a smaller reporting company that is also classified as an accelerated filer, we are subject to certain disclosure and compliance requirements that apply to other public companies that did not previously apply to us due to our status as an EGC. These requirements include, but are not limited to: • the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404 (b) of the Sarbanes- Oxley Act of 2002 (" Section 404 "); and • the requirement that we hold a non- binding advisory vote on executive compensation, the frequency of such advisory vote on executive compensation, and obtain stockholder approval of any golden parachute payments not previously approved. We expect that compliance with these additional requirements will increase our legal and financial compliance costs and may cause management and other personnel to divert attention from operational and other business matters to devote increased time to public company reporting requirements. In addition, if we are not able to comply with changing requirements in a timely manner, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The Nasdaq Stock Market LLC, the SEC or other regulatory authorities, which would require additional financial and management resources.~~ If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock. The Sarbanes- Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. We are required, under Section 404, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Section 404 also generally requires an attestation from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. ~~While~~ **As a public company and large accelerated filer for the year ended December 31, 2022,** we were **required to provide management' s attestation on internal controls pursuant to Section 404 of the Sarbanes- Oxley Act,** ~~an~~ **and** ~~EGC,~~ our independent registered public accounting firm was ~~not~~ required to attest to the effectiveness of our internal ~~controls~~ **control** over financial reporting pursuant to Section 404 **of the Sarbanes- Oxley Act** . ~~This exemption~~ **However, as of the last business day of our second fiscal quarter of 2023, we determined that we requalify as a smaller reporting company and as a non-accelerated filer for the year ended December 31, 2023. We are therefore** no longer ~~applies~~ **required** to ~~us as of December 31, 2022. Accordingly, beginning with~~ **include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm in** this Annual Report on Form 10- K **for** ~~, we are required to include an attestation from our independent registered public accounting firm on~~ the **fiscal year ended December 31, 2023** ~~effectiveness of our internal control over financial reporting~~ . Our compliance with Section 404 ~~will~~ **in future periods may** require that we incur substantial expense and expend significant management efforts. We currently do not have an internal audit group, and rely on experienced consultants to support this function. We may need to hire additional consultants or accounting and financial staff with appropriate public company experience and technical accounting knowledge in order to continually comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or

if our independent registered public accounting firm determines we have a material weakness ~~or significant deficiency~~ in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The Nasdaq Stock Market LLC, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets. Risks Related to the Ownership of Our Common Stock and Other General Matters The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our common stock. The market price of our common stock has been and likely will remain volatile. The stock market in general and the market for biopharmaceutical or pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies ~~, including very recently in connection with the ongoing COVID- 19 pandemic~~ , which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to new or ongoing public health crises or other inflationary factors, may negatively affect the market price of our common stock, regardless of our actual operating performance. As a result of this volatility, you may lose all or part of your investment in our common stock since you might be unable to sell your shares at or above the price you paid for the shares. The market price for our common stock may be influenced by many factors, including: • results of clinical trials of our current and any future drug candidates or those of our competitors; • the success of competitive drugs or therapies; • 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; • the level of expenses related to our current and any future drug candidates or clinical development programs; • the results of our efforts to discover, develop, acquire or in- license additional drug candidates; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices; • disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • significant lawsuits, including patent or stockholder litigation; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • general economic, industry and market conditions; and • the other factors described in this " Risk Factors " section. In addition, in the past, stockholders have initiated class action lawsuits against companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management' s attention and resources. Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price. The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, increases in inflation rates and uncertainty about economic stability. **Global geopolitical tensions have** ~~For example, the COVID- 19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. Similarly, the Russia- Ukraine war has~~ created extreme volatility in the global capital markets and ~~is~~ **are** expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. There is no public market for our Series A convertible preferred stock. There is no established public trading market for our Series A convertible preferred stock, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the Series A convertible preferred stock on any national securities exchange or other nationally recognized trading system. Without an active market, the liquidity of the Series A convertible preferred stock will be limited. We may sell additional equity or debt securities or enter into other arrangements to fund our operations, which may result in dilution to our stockholders and impose restrictions or limitations on our business. Until such time as we can generate substantial revenue from drug sales, if ever, we expect to finance our cash needs through a combination of equity and debt financings, strategic alliances, and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. To the extent that we issue additional equity securities, our stockholders may experience substantial dilution, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. In addition, we may issue equity or debt securities as consideration for obtaining rights to additional compounds. In November 2020, we filed a shelf registration statement on Form S- 3 (Registration No. 333- 250054) **(the " Prior Registration Statement "). In November 2023, upon expiration of the of the Prior Registration Statement, we filed a new shelf registration statement on Form S- 3 (Registration No. 333- 275307)** that allows us to sell up to an aggregate of $ 250. 0 million of our common stock, preferred stock, debt securities and / or warrants (the " **Current** S- 3 Registration Statement "), which includes a prospectus covering the issuance and sale of up to $ 75. 0 million of common stock pursuant to an at- the- market (" ATM ") offering program. As of December 31, ~~2022~~ **2023** , we had $ 250. 0 million available under our **Current** S- 3 Registration Statement, including $ 75. 0 million available pursuant to our ATM program. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, issuing additional equity, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could negatively impact our ability to conduct our business. If we raise additional capital through future collaborations, strategic alliances or third- party licensing arrangements, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research

programs or drug candidates, or grant licenses on terms that may not be favorable to us. Any of these events could significantly harm our business, financial condition and prospects. You will be diluted by any conversions of outstanding Series A convertible preferred stock and exercises of outstanding options. As of December 31, ~~2022~~ **2023**, we had outstanding options to purchase an aggregate of **15,** ~~12~~ **124**, **546** ~~961, 238~~ shares of our common stock at a weighted average exercise price of $ ~~4~~ **3**. ~~13~~ **87** per share and 1, 250, 000 shares of common stock issuable upon conversion of outstanding Series A convertible preferred stock for no additional consideration. Such Series A convertible preferred stock is convertible any time at the option of the holder thereof subject to the beneficial ownership limitations described in Note 7 to the **consolidated** financial statements contained in this Annual Report on Form 10- K. The exercise of such options and conversion of the Series A convertible preferred stock for shares of our common stock will result in further dilution of your investment and could negatively affect the market price of our common stock. In addition, you may experience further dilution if we issue common stock, or securities convertible into common stock, in the future. As a result of this dilution, you may receive significantly less than the full purchase price you paid for the shares in the event of liquidation. Concentration of ownership of our common stock among our executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions. Based upon shares of our common stock outstanding as of December 31, ~~2022~~ **2023**, our executive officers, directors and stockholders who owned more than 5 % of our outstanding common stock, in the aggregate, beneficially own shares representing approximately ~~45~~ **52**. ~~2~~ **4** % of our outstanding common stock. Takeda, a greater than 5 % holder, has agreed to, among other things, (i) a standstill provision, (ii) restrictions on its ability to sell or otherwise transfer its shares of our stock, (iii) vote its shares on certain matters in accordance with the holders of a majority of shares of our common stock and (iv) restrictions on the percentage of our outstanding common stock it may own, in accordance with the terms of the RLT Agreement. If our executive officers, directors and stockholders who owned more than 5 % of our outstanding common stock acted together, they may be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power, Takeda standstill provisions, voting obligations and transfer restrictions could delay or prevent an acquisition of our company on terms that other stockholders may desire or result in the management of our company in ways with which other stockholders disagree ~~with~~. 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 relies, in part, on the research and reports that industry or financial analysts publish about us or our business. We do currently have research coverage offered by several industry or financial analysts, although two analysts have withdrawn research coverage recently. We do not have any control over these analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If additional analysts cease to cover our stock or fail to regularly publish reports, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions: • establish a classified board of directors such that not all members of the board are elected at one time; • allow the authorized number of our directors to be changed only by resolution of our board of directors; • limit the manner in which stockholders can remove directors from the board; • establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors; • require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent; • limit who may call stockholder meetings; • authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so- called “ poison pill, ” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and • require the approval of the holders of at least 66 2 / 3 % of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Additionally, the Takeda standstill provisions and transfer restrictions in the RLT Agreement may delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. We may be subject to securities litigation, which is expensive and could divert management attention. The market price of our common stock may be volatile. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management’ s attention from other business concerns, which could

seriously harm our business. Some provisions of our charter documents and Delaware law may have anti- takeover effects that could discourage an acquisition of us by others, even if an acquisition would benefit our stockholders and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. These provisions include: • authorizing the issuance of " blank check " preferred stock, the terms of which we may establish and shares of which we may issue without stockholder approval; • prohibiting cumulative voting in the election of directors, which would otherwise allow for less than a majority of stockholders to elect director candidates; • prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders; • eliminating the ability of stockholders to call a special meeting of stockholders; and • establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings. These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law (the " DGCL "), which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under the DGCL, a corporation may not, in general, engage in a business combination with any holder of 15 % or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change of control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock. Sales of a substantial number of shares of our common stock in the public market could cause the market price of our common stock to drop significantly. 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 intend to sell shares, could reduce the market price of our common stock. Some of the holders of our securities have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares would result in the shares becoming freely tradable without restriction under the Securities Act except for shares held by our affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.