Risk Factors Comparison 2024-06-11 to 2023-06-28 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with the other information in this Annual Report, including our Consolidated Financial Statements and the related notes included in this Annual Report and in the section titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " before deciding whether to invest in our securities. The ~~cost~~ **occurrence** of ~~pharmaceuticals continues to generate substantial governmental and third- party payer interest, and pharmaceutical pricing and marketing currently received a great deal of Congressional and administrative attention. There have been numerous initiatives on~~ **one** ~~the federal and state levels in the U. S. for~~ **or more of** ~~comprehensive reforms affecting~~ the payment **events** ~~for~~ **or circumstances described in** ~~, the availability of, and reimbursement for, healthcare services. In particular, there~~ **these risk factors** ~~have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products~~, **alone** ~~limiting coverage and reimbursement for~~ **or** ~~drugs and~~ **in combination with** other **events** ~~medical products, government control and other changes to the healthcare system in the U. S. Congressional inquiries and proposed and enacted federal and state legislation have also been released and are designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for~~ **or circumstances** ~~drugs. Recent federal budget proposals have included measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B~~ , ~~to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low- income patients. Current and future U. S. legislative healthcare reforms~~ may ~~result in price controls and other restrictions for any approved products, if covered, and could seriously harm our business. Drug pricing reform policies may be pursued in the future and may be more aggressive, regardless of which party controls the White House. Given that drug pricing controls is a key legislative and administration priority, it is likely that additional pricing controls will be enacted and could harm our business, financial condition and results of operations. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states, such as California, have enacted transparency laws that require manufacturers to report drug price increases and related information. The boom in state laws targeting drug pricing is unprecedented and the requirements are not uniform from state to state, creating additional compliance and commercialization challenges for manufacturers. We further expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations, judicial interpretation of health care reform efforts, and additional legislative and regulatory proposals resulting in ongoing, relatively rapid changes to applicable laws and regulations. Our results of operations could be adversely affected by current and future healthcare reforms. 33 Government and private payers also increasingly require pre - approval of coverage for new or innovative devices or drug therapies or condition coverage on unsuccessful alternative treatment before they will reimburse healthcare providers that use such therapies. For some specialty drugs, payers are conditioning payment on successful treatment measured by objective metrics. While we cannot predict whether any proposed cost - containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could~~ have a material adverse effect on our **business** ~~ability to obtain adequate prices for our product candidates and operate profitably. As in the past~~ , **reputation, revenue, financial condition,** ~~there may be other efforts to repeal or materially modify various aspects of ACA. The~~ results ~~and effects~~ of **operations** ~~such efforts, including judicial~~ and ~~Congressional challenges~~ **future prospects** , **in which event the market price of our common stock** could ~~affect~~ **decline, and you could lose part or all of your investment. Unless otherwise indicated, reference in this section and elsewhere in this Annual Report to** our business **being adversely affected** ~~operations and prospects in unknown ways. Also~~ , **negatively impacted or harmed** ~~it is unclear how ACA and other laws ultimately~~ will ~~be fully implemented or modified. For example, in the case of Texas v. Azar, a federal district court in Texas struck down the ACA in its entirety, finding that the Tax Cuts and Jobs Act of 2017 rendered the individual mandate unconstitutional. The December 15, 2019, opinion concluded~~ - **include** ~~that since the individual mandate is " essential " to the ACA, it could not be severed from the rest of the ACA and therefore, the entire ACA was unconstitutional. Despite its decision, however, the court did not issue~~ an ~~injunction and therefore, immediate compliance was not required. Following appeal of the Fifth Circuit' s decision upholding the ruling of the federal district court, on June 17, 2021, the Supreme Court reversed the decision of the Fifth Circuit, which vacated the judgment and instructed the lower court to dismiss the case. Despite the Supreme Court' s recent ruling in California v. Texas (formerly Texas v. Azar), it remains unclear how future decisions from the Supreme Court and the various other courts across the country, if any, to repeal and replace the ACA will impact the ACA and our business. It is also unclear how regulations and sub- regulatory policy, which fluctuate continually, may affect interpretation and implementation of the ACA and its practical effects on our business. In the future, there may continue to be additional proposals relating to the reform of the U. S. healthcare system, some of which could further limit the prices we will be able to charge for our product candidates, or the amounts of reimbursement available for our product candidates. If future legislation were to impose direct governmental price controls or access restrictions, it could have a significant adverse impact on our business. Additionally, with the change in administration it is possible that President Biden may issue Executive Orders with the potential to change a number of prior executive branch~~

~~actions on drug pricing. We continue to monitor the potential impact of proposals to lower prescription drug costs at the federal and state level. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, measures to reduce costs of the Medicaid program, and some states are considering implementing measures that would apply to broader segments of their populations that are not Medicaid- eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payer or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability. These and other healthcare reform initiatives may result in additional reductions in Medicare and other healthcare funding, which could have a material~~ adverse effect on **,** ~~our~~ **or a negative impact or harm to, the business, reputation,** financial **condition, results of** operations **, revenue and our future prospects** ~~. We expect~~ **The material and other risks and uncertainties summarized elsewhere in this Annual Report and described below are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us, or** that ~~additional state~~ **we currently deem immaterial, may also impair our business operations. This Annual Report also contains forward- looking statements that involve risks** and ~~federal healthcare reform measures will~~ **uncertainties. Our actual results could differ materially from those anticipated in the forward- looking statements as a result of a number of factors, including the risks described below. See the section titled " Forward- Looking Statements. " • the successful completion of clinical or nonclinical studies in any of our development programs may not** be ~~adopted in~~ **sufficient to cause** the ~~future,~~ **FDA to approve** any **NDA** ~~of which could limit the amounts~~ that **we may submit,** ~~federal and state governments will pay for~~ **or cause any other agency to provide regulatory approval of any of** ~~healthcare products and services, which could result in reduced demand for~~ our product candidates ~~or additional pricing pressures. 34 The Foreign Corrupt Practices Act The Foreign Corrupt Practices Act (FCPA) prohibits any U. S. individual or business from paying~~ , offering, or authorizing payment or offering....., and to devise and maintain an **and** ~~adequate system of internal accounting controls for international operations. Activities that violate the FCPA~~ , even if ~~they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts. Foreign Regulation To the extent we choose to develop or sell any products outside of the U. S., we will be subject to a variety of foreign regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales, and distribution of our products. For example, in the European Union (EU) we must obtain authorization of a clinical trial application in each member state in which we intend to conduct a clinical trial. Whether or not we obtain U. S. FDA approval~~ **approved** ~~for a product~~ , ~~we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain U. S. FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country. Regulatory approval in one country~~ does not ensure ~~regulatory approval in another, but~~ **acceptance of such product candidates by clinicians leading to** a **revenue stream** ~~failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. As in the U. S., post - approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution, would apply to any product that is approved outside the U. S. Subsidiaries and Inter- Corporate Relationships As of March 31, 2023, we had two~~ **to support our** ~~wholly- owned subsidiaries, Pherin Pharmaceuticals, Inc., a Delaware corporation, and Vistastem Inc., a California corporation. The~~ operations ~~of these subsidiaries are managed by our senior management team based in South San Francisco, California. Corporate History Vistastem, Inc., a California corporation (formerly VistaGen Therapeutics, Inc.) was incorporated on May 26, 1998, and is our wholly- owned subsidiary. Excaliber Enterprises, Ltd. (Excaliber), a publicly- held company (formerly OTCBB: EXCA) was incorporated under the laws of the State of Nevada on October 6, 2005. Pursuant to a strategic merger transaction on May 11, 2011, Excaliber acquired all outstanding shares of Vistastem in exchange for 341, 823 shares of our common stock and assumed all of Vistastem' s pre- Merger obligations (the Merger). Shortly after the Merger, Excaliber' s name was changed to " Vistagen Therapeutics, Inc. " (a Nevada corporation). Vistastem, as the accounting acquirer in the Merger, recorded the Merger as the issuance of common stock for the net monetary assets of Excaliber, accompanied by a recapitalization. The accounting treatment for the Merger was identical to that resulting from a reverse acquisition, except that we recorded no goodwill or other intangible assets. A total of 78, 450 shares of our common stock, representing the shares held by stockholders of Excaliber immediately prior to the Merger are reflected as outstanding for all periods presented in the Consolidated Financial Statements of the Company included in Item 8 of this Annual Report. Additionally, the Consolidated Balance Sheets reflect the $ 0. 001 par value of Excaliber' s common stock. 35 On December 20, 2022, we entered into an Agreement and Plan of Merger (the Merger Agreement) along with VTGN Merger Sub, Inc., our wholly- owned subsidiary (Merger Sub), Pherin Pharmaceuticals, Inc. (Pherin), and Kevin McCarthy in his capacity of Stockholder Representative, in order to acquire Pherin (the Pherin Acquisition). On February 2, 2023 (the Closing Date), we completed the Pherin Acquisition and Pherin is now a wholly- owned subsidiary of the Company. Immediately prior to the consummation of the Pherin Acquisition, each of Pherin' s directors and officers resigned, and no employees or other affiliates of Pherin on the Closing Date are serving or will serve in their previous roles or in any other capacity with Pherin or with the Company. Following the completion of the Pherin Acquisition, we now have full ownership of intellectual property rights to all five of our pherine drug candidates. The Consolidated Financial Statements included in Item 8 of this Annual Report represent the activity of Vistastem from May 26, 1998, the consolidated activity of Vistastem and Excaliber (now Vistagen Therapeutics, Inc., a Nevada corporation), from May 11, 2011 (the date of the Merger) through March 31, 2023, and the activity of Pherin Pharmaceuticals, Inc. from February 2, 2023 (the date of the Pherin Acquisition) through March 31, 2023. For the relevant periods, the Consolidated Financial Statements included in Item 8 of this Annual Report also include the accounts of Vistastem'~~

~~s two wholly owned inactive subsidiaries, Artemis Neuroscience, Inc., a Maryland corporation which was dissolved in April 2022, and VistaStem Canada, Inc., a corporation organized under the laws of Ontario, Canada which was dissolved in June 2022. Research and Development Conducting research and development is central to our business model. We have invested and expect to continue to invest significant time and capital in our research and development operations. Our research and development expenses were approximately $ 44. 4 million and $ 35. 4 million for the fiscal years ended March 31, 2023 and 2022, respectively. We expect that our research and development expenses will remain a significant portion of our total operating costs for the foreseeable future as we seek to complete the development of fasedienol, itruvone, and AV- 101 and our other recently acquired pherine product candidates. Environmental, Social, Governance, and Human Capital We believe corporate responsibility is fundamental to our mission and we are committed to holding ourselves to high ethical standards. Beyond our quest to develop innovative therapeutic solutions that combat CNS disorders affecting so many lives and to improve healthcare outcomes, we strive to have a positive impact on our employees, our local communities, our patients, our shareholders, the health care ecosystem and society as a whole. Governance and Leadership As a late- clinical stage company that is passionate about transforming mental health care, we believe creating an environment that allows our team to collectively thrive and achieve its full potential begins with our Board of Directors, which consists of directors with diverse and dynamic backgrounds in pharmaceutical development, commercialization, and corporate governance. Applying the Nasdaq Stock Market' s continued listing standards for director independence, five of our seven directors are currently independent. At the management level, we have built a team of highly experienced professionals that we believe provide us with a diverse and inclusive culture, while also providing the know- how necessary to allow us to achieve our short- and long- term goals. Among these goals is to develop a formal environmental, social and governance (ESG) strategic roadmap and framework that will guide our operations, so as to ensure that we are operating in a manner that is consistent with our mission of transforming mental health care — One Mind at a Time. Core Values and Ethics We are committed to driving improvement and innovation in the care of patients suffering from CNS disorders. In this pursuit, our core values of integrity, compassion, teamwork, and excellence while on our journey to change the way we approach mental healthcare guide our internal processes and define our mission to radically improve mental health and well- being worldwide. In addition, all of our directors, officers and employees are responsible for upholding these values as set forth in our Code of Business Conduct and Ethics, which forms the foundation of our policies and practices. Our Code of Business Conduct and Ethics is available on our website at www. vistagen. com. 36 Environmental Commitment We are committed to protecting the environment and attempt to mitigate any negative impact of our operations. We strive to address the environmental impacts of the building in which we operate and minimize waste by reducing our use of paper by operating primarily in a digital environment. We have safety protocols in place for handling biohazardous waste in our labs, and we use third- party vendors for biohazardous waste and chemical disposal. Human Capital and Employees We believe that our people are one of our greatest assets. We make diversity and inclusion priorities because they are key to unlocking the potential of our people. With colleagues who can contribute unique viewpoints and diverse perspectives to all aspects of the business, we believe that our culture can be more collaborative, more accepting of difference and more prepared for overall success on our journey to reimage medicine. As of June 28, 2023, we employed 33 full- time employees and one part- time employee. Twenty- one full- time employees work in research and development and laboratory support services and twelve full- time employees work in management, business development, legal, human resources, general and administrative roles. Staffing for other functional areas is achieved through our diverse network of strategic relationships with multiple CROs, CDMOs, and other third- party service providers and consultants. These service providers and consultants provide us with support services on a flexible, real- time, as- needed basis, including services related to, among others, payroll, information technology, legal, investor and public relations, manufacturing, product development, regulatory affairs and FDA program management to complement our internal resources in these areas. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective bargaining agreement. We consider our employee relations to be good. Facilities We lease our office and laboratory space, which consists of approximately 10, 900 square feet located in South San Francisco, California, under a lease expiring on July 31, 2027 which also provides a five- year option to renew. Legal Proceedings None. Available Information We file reports and other information with the SEC, as required by the Exchange Act. We make available free of charge through our website (http: / / www. vistagen. com) our annual reports on Form 10- K, quarterly reports on Form 10- Q, current reports on Form 8- K and amendments to those reports filed or furnished pursuant to Sections 13 (a) and 15 (d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled " Investors, " as a source of information about us. The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10- K by reference. 37 Item 1A. Risk Factors Risk Factor Summary Our business is subject to substantial risk and an investment in our securities involves various risks. Some of the material risks include those set forth below. You should consider carefully these risks, and those discussed under " Risk Factors " below, before investing in our securities. These risks include, among others: ● we require substantial additional financing to execute our long- term business plan either on our own or with collaborators, including further development of our product candidates ; ● We • we~~ have incurred significant net losses since inception **,** and we will continue to incur substantial operating losses for the foreseeable future; ●~~–~~• we are a ~~development~~ **clinical-** stage biopharmaceutical company with no revenues from product sales or approved products, and limited experience developing new drug candidates, which makes it difficult to assess our future viability; ●~~–~~• **we require additional financing to execute our long- term business plan, including further development and potential commercialization of our product candidates; • raising additional capital in equity- based financing transactions is likely to cause substantial dilution to our existing stockholders, may restrict our operations or require us to relinquish rights,**

and may require us to seek stockholder approval to authorize additional shares of our common stock; • failures of ~~our current and / or~~ future clinical studies of our product candidates, or delays in the commencement ~~of~~ **or** completion of our **ongoing or planned** clinical trials, could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business; ~~● •~~ we depend heavily on the success of our product candidates **,** and we cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, any of our current or future product candidates; ~~● •~~ if we are unable to retain or attract key management and scientific personnel, we may be unable to successfully produce ~~and~~ **,** develop **, and commercialize** our product candidates; ~~• ● the successful completion of clinical or nonclinical studies in any of our development programs may not be sufficient to cause the FDA to approve of any NDA that we may submit or cause any other agency to provide regulatory approval of any of our product candidates and, even if approved, does not ensure acceptance of such product candidates by clinicians leading to a revenue stream to support our operations; ●~~ we face significant competition, and if we are unable to compete effectively, we may not be able to achieve or maintain significant market penetration or improve our results of operations; ~~● •~~ if we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects; ~~● raising additional capital in equity- based financing transactions is likely to cause substantial dilution to our existing stockholders, may restrict our operations or require us to relinquish rights,~~ and ~~• may require us to seek stockholder approval to authorize additional shares of our common stock; ● if we fail to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted; and ●~~ other risks and uncertainties, including those described under Risk Factors below. If we are unable to effectively manage the impact of these and other risks, our ability to operate and execute our business plan would be substantially impaired. In turn, the value of our securities would be materially reduced. ~~38 You should consider carefully the risks~~ **Risks** ~~and~~ **Related to Our Business The successful development of pharmaceutical products is highly** ~~uncertainties~~ ~~----~~ **uncertain** ~~described below~~ **. Successful development of pharmaceutical products is highly uncertain and is dependent on numerous factors** , **many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including: • clinical trial results may show the product candidates to be less effective than expected (for example, a clinical trial could fail to meet its primary or key secondary endpoint (s)) or have an unacceptable safety or tolerability profile; • failure to receive the necessary regulatory approvals or a delay in receiving such approvals, which, among** ~~together~~ ~~---~~ **other things, may be caused by patients who fail the trial screening process, slow enrollment in clinical trials, patients dropping out of trials, patients lost to follow- up, length of time to achieve trial endpoints, additional time requirements for data analysis, review of IND, NDA or similar foreign applications, preparation, discussions** with ~~all~~ **the FDA or foreign regulatory authorities, an FDA or foreign regulatory authority request for additional preclinical or clinical data (such as long- term toxicology studies) or unexpected safety or manufacturing issues; • preclinical study results may show the product candidate to be less effective than desired or to have harmful side effects; • post- marketing approval requirements; or • the proprietary rights** of **others and** ~~the~~ **their competing products and technologies that may prevent our product candidates from being commercialized. The length of time necessary to complete clinical trials and submit an application for marketing approval for a final decision by a regulatory authority varies significantly from one product candidate to the next and from one country or jurisdiction to the next and may be difficult to predict. Even if we are successful in obtaining marketing approval, commercial success of any approved products will also depend in large part on the availability of coverage and adequate reimbursement from third- party payors, including government payors such as the Medicare and Medicaid programs and managed care organizations in the U. S. or country- specific governmental organizations in foreign countries, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third- party payors could require us to conduct additional studies, including post- marketing studies related to the cost effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and** other **healthcare payors were not to provide coverage and adequate reimbursement for our products once approved, market acceptance and commercial success would be reduced. In addition, if any of our product candidates receive marketing approval, we will be subject to significant regulatory obligations regarding the submission of safety and other post- marketing** information **and** ~~in this Report~~ **reports** ~~before investing in~~ **and registration, and will need to continue to comply (** ~~our~~ **or ensure** ~~securities. The risks described below are not the only risks facing our Company. Additional risks and uncertainties not currently known to us or~~ that ~~we~~ **our third- party providers comply) with** ~~currently~~ ~~--~~ **current** ~~deem~~ **cGMPs and similar foreign requirements, and GCPs for any clinical trials that we conduct post- approval. In addition, there is always the risk that we, a regulatory authority or a third party might identify previously unknown problems with a product post- approval, such as adverse events of unanticipated severity or frequency. Compliance with these requirements is costly, and any failure** to ~~be immaterial may also materially~~ **comply or other issues with our product candidates post- approval could** adversely affect our business, financial condition and ~~/ or operating~~ results **of operations. Our business is highly dependent on the success of our product candidates. If we are unable to successfully complete clinical development, obtain regulatory approval for or commercialize one or more of our product candidates, or if we experience delays in doing so, our business will be materially harmed. To date, as an organization, we have not completed the development of any of our product candidates. Our future success and ability to generate revenue from our product candidates is dependent on our ability to successfully develop, obtain regulatory approval for and commercialize one or more of our product candidates. All of our product candidates will require substantial additional investment for clinical development, regulatory review and approval in one or more jurisdictions** . If any of **our product candidates encounters safety** ~~the following risks are realized, our~~ ~~-~~ **or efficacy problems, development**

delays or regulatory issues or other problems, our development plans and business ~~, financial condition and results of operations could~~ **would** be materially **harmed. We may not have the financial resources to continue development of our product candidates if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our product candidates, including: • our inability to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe** and **effective; • insufficiency of our financial and other resources to complete the necessary preclinical studies, clinical trials and regulatory submissions; • negative or inconclusive results from our preclinical studies, clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical studies, clinical trials or abandon a program; • product- related** ~~adversely~~ -- **adverse** ~~affected~~ **events experienced by subjects in our clinical trials, including unexpected toxicity results, or by individuals using drugs or therapeutic biologics similar to our product candidates; • delays in submitting an IND or comparable foreign applications or delays or failure in obtaining the necessary approvals or allowances from regulators to commence a clinical trial or a suspension or termination, or hold, of a clinical trial once commenced; • conditions imposed by the FDA or comparable foreign regulatory authorities regarding the scope or design of our clinical trials; • poor effectiveness of our product candidates observed during clinical trials; • better than expected performance of control arms, such as placebo groups, which could lead to negative or inconclusive results from our clinical trials; • delays in enrolling subjects in our clinical trials; • high drop- out rates of subjects from our clinical trials; • inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials; • higher than anticipated clinical trial or manufacturing costs; • unfavorable FDA or comparable regulatory authority inspection and review of our clinical trial sites; • failure of our third- party contractors or investigators to comply with regulatory requirements or the clinical trial protocol or otherwise meet their contractual obligations in a timely manner, or at all; • delays and changes in regulatory requirements, policies and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our therapies in particular; or • varying interpretations of data by the FDA and comparable foreign regulatory authorities** . We are a ~~development~~ **clinical** - stage biopharmaceutical company with no recurring revenues from product sales or approved products ~~,~~ **. We are not profitable** and ~~limited experience~~ **have incurred losses in each period since our inception. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and** ~~developing~~ **development** ~~new therapeutic~~ **of, and seek regulatory approvals for, and commercialization of our** product candidates ~~, including conducting clinical trials and other areas required for the successful development of therapeutic products, which makes it difficult to assess our future viability~~ . We are a ~~development~~ **clinical** - stage biopharmaceutical company. We ~~currently~~ have no **products** approved ~~products~~ **for commercial sale** and **have generated** no revenue from product sales ~~,~~ **to date. We will continue to incur significant research** and **development and other expenses related to our preclinical and clinical development and ongoing operations. As a result,** we **are not profitable and** have ~~not yet fully demonstrated~~ **incurred losses in each period since our inception. Net losses and negative cash flows have had, and will continue to have,** an ~~ability~~ **adverse effect on our stockholders' equity and working capital. Our net losses totaled $ 29. 4 million and $ 59. 2 million for the years ended March 31, 2024 and 2023, respectively. We expect** to ~~overcome~~ **continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, and commercialization of our product candidates. We anticipate that our expenses will increase substantially if, and as, we: • advance our product candidates through clinical development, including as we advance these candidates into and through later- stage clinical trials; • seek regulatory approvals for** ~~many~~ - **any** ~~of~~ **product candidates that successfully complete clinical trials; • hire additional clinical, quality control, medical, scientific and** ~~the~~ **other** ~~fundamental~~ **technical personnel to support the clinical development of our product candidates; • experience an increase in headcount as we expand our research and development organization and market development and pre- commercial planning activities; • undertake any pre- commercial or commercial activities to establish sales, marketing and distribution capabilities; • advance our preclinical- stage product candidates into clinical development; and • maintain, expand and protect our intellectual property portfolio. Biopharmaceutical product development entails substantial upfront capital expenditures and significant** ~~risks~~ - **risk that any potential product candidate will fail to demonstrate adequate efficacy or** ~~and~~ - **an acceptable safety profile, gain regulatory approval, secure market access and reimbursement, and become commercially viable, and therefore any investment in us is highly speculative. Accordingly, before making an investment in us, you should consider our prospects, factoring in the costs,** uncertainties **, delays and difficulties** frequently encountered by **companies in clinical** development **, especially clinical-** stage **biopharmaceutical** companies **such as ours** ~~in new and rapidly evolving fields of technology, particularly biotechnology~~ . ~~To~~ **Any predictions you make about our future success or viability may not be as accurate as they would otherwise be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. Additionally, our expenses could increase beyond our expectations if we are required by the FDA or other regulatory authorities to perform preclinical studies or clinical trials in addition to those that we currently anticipate, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of any of our product candidates. We have never generated revenue from product sales and may never be profitable. Our ability to become and remain profitable depends on our ability to generate revenue or** execute ~~our~~ **other** business ~~plan~~ **development arrangements. We do not expect to generate significant revenue, if any, unless and until we are able to obtain regulatory approval for, and** successfully **commercialize** , **one or more product candidates** we **are developing or may develop. Successful commercialization will require achievement of many key milestones, including demonstrating sufficient evidence of safety and efficacy in clinical trials,**

obtaining regulatory approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain regulatory approval, satisfying any post- marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any further losses or if or when we might achieve profitability. We may never succeed in these activities, and even if we do, we may never generate revenues that are significant enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable may depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to incur losses as we have since our inception, investors may not receive any return on their investment and may lose their entire investment. We will need **substantial** ~~to accomplish or continue to accomplish the following fundamental objectives, either on our own or with collaborators: ● develop and obtain required regulatory approvals for commercialization of any of our product candidates; ● maintain, leverage and expand our intellectual property portfolio; ● gain market acceptance for our product candidates; and ● obtain adequate capital resources and manage our spending as costs and expenses increase due to research, production, development and regulatory approval of product candidates. We require~~ additional financing to execute our long- term business plan ~~. From~~ **, and if we are unable to raise capital when needed, we could be forced to delay, reduce** ~~our~~ **or terminate our research and development programs or pre- commercialization efforts. Our operations have consumed substantial amounts of cash since** inception ~~through 2019, a~~ **. As in prior periods we expect to continue to spend** substantial ~~portion~~ **amounts** of **cash** ~~our resources were dedicated~~ to ~~research~~ **continue the preclinical** and ~~development of AV- 101 and Vistastem's stem cell technology platform. Since 2019, we have expended a considerable portion of our resources for research,~~ clinical development ~~, manufacturing and regulatory expense related to fasedienol and itruvone, including costs related to the PALISADE Phase 3 Program and our Phase 1 study~~ of ~~itruvone in MDD. We expect to continue to expend substantial resources for the foreseeable future developing fasedienol, itruvone, AV- 101 and~~ our ~~other~~ product candidates ~~, PH15, PH80 and PH284, on our own and in collaborations~~ . These expenditures will include costs associated with general and administrative costs, facilities costs, research and development, ~~acquiring new technologies,~~ manufacturing ~~product candidates~~ , conducting nonclinical experiments and clinical trials ~~and~~ **,** obtaining regulatory approvals **and commercialization,** should the FDA approve any of ~~such~~ **our** product candidates for sale. **We** ~~Although we had cash and cash equivalents of approximately $ 16. 6 million at March 31, 2023, we have not yet developed products that generate recurring revenue and, assuming successful completion of our planned clinical and nonclinical programs, we~~ will need to ~~invest~~ **raise** substantial additional capital ~~resources~~ to ~~commercialize any of them. During the next twelve months, subject to availability of adequate working capital, we plan to (i) continue to advance our FEARLESS Phase 3 Program, on our own or with a collaborator, to develop and commercialize fasedienol as a new acute treatment of anxiety in adults with SAD, (ii)~~ complete **certain of** ~~preparations, on our own or~~ **our currently planned preclinical** ~~with a collaborator, for~~ and ~~initiate further Phase 2B~~ clinical development **programs, including future late** ~~of itruvone as a potential stand- alone treatment~~ **stage clinical trials. If we are able to gain marketing approval** for ~~MDD~~ **any product candidates that we develop** , ~~(iii)~~ **we will require significant amounts of additional capital in order to launch and commercialize such product candidates. As the outcome of our ongoing research and development activities, including the outcome of future anticipated preclinical studies and clinical trials, is highly uncertain, we cannot reasonably estimate the actual amounts of additional capital necessary to successfully** complete **the** ~~IND- enabling activities, either on our own with a collaborator, for Phase 2B~~ development ~~of PH80, PH15~~ and **commercialization** ~~PH284 and Phase 2A development~~ of **any** ~~AV- 101 for one or more neurological disorders involving the NMDAR, and (iv) conduct various nonclinical studies involving each of our~~ product ~~candidates~~ **candidate** ~~. 39 Although~~ we **develop. We** ~~received the $ 5 million upfront payment under the AffaMed Agreement in August 2020 and expect to recognize that amount as revenue in future periods, we have no other source of revenue or recurring cash flows from product sales to sustain our present activities, and we~~ do not expect to generate sustainable positive operating cash flows until, and unless, we ~~(i) out- license or sell a product candidate to a third- party that is subsequently successfully developed and commercialized, (ii) enter into additional transactions involving our stem cell technology, or (iii)~~ obtain approval from the FDA and other regulatory authorities and successfully commercialize ~~fasedienol, or~~ one ~~of our~~ **or** ~~other~~ **more of our** product candidates ~~, on our own or through collaborations. As the outcome of our ongoing research and development activities, including the outcome of future anticipated nonclinical studies and clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any of our product candidates, on our own or in collaboration with others. As in prior periods, we will continue to incur substantial costs associated with other clinical and nonclinical development programs for our product candidates. In addition, other unanticipated costs may arise~~ . As a result of these and other factors, we will need to seek additional capital to meet our future operating plans and requirements, including capital necessary to develop, obtain regulatory approval for **, and commercialize** fasedienol and our other product candidates, and may seek additional capital in the event there exists favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans and requirements ~~We have completed in the past a range of potential financing transactions, including public or private equity or debt financings, government or other third- party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches, and we intend to pursue and complete additional financing arrangements in the future~~ . Our future ~~capital requirements may~~ **need for additional funding** ~~depend~~ **depends** on many factors, including: ~~●~~ • the number and characteristics of ~~the~~ **future** product candidates we pursue **and their development requirements** ; ~~●~~ • the scope, progress, results and costs of researching, developing and commercializing our product candidates ~~,~~ and ~~conducting preclinical~~ **any other additional product candidates we may develop** and ~~clinical studies ●~~ **pursue in the future; •** the timing of, and the costs involved in, obtaining ~~regulatory~~ **marketing**

approvals for our product candidates **and any other additional product candidates we may develop and pursue in the future** ; ~~● •~~ **subject to receipt of regulatory approval, the costs of commercialization activities for our product candidates, to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities; • subject to receipt of regulatory approval, revenue, if any, received from commercial sales of our product candidates or any other additional product candidates we may develop and pursue in the future; •** the cost of manufacturing and formulating our product candidates; ~~● our ability~~ **• the extent** to **which we** establish and maintain strategic partnerships, licensing or other collaborative arrangements ~~and~~ **for** the **development of our product candidates, on favorable** financial terms ~~of such agreements~~ **, if at all** ; ~~● •~~ **subject to regulatory approval,** market acceptance of our product candidates; ~~● •~~ the effect of competing technological and market developments; ~~● •~~ our ~~ability to obtain government funding for~~ **headcount growth and associated costs as we expand** our research and development ~~programs~~ **and market development and pre- commercial planning activities** ; ~~● •~~ the costs ~~involved in obtaining~~ **of preparing, filing and prosecuting patent applications** , maintaining and **protecting** ~~enforcing patents to preserve our intellectual property; ● the costs involved in defending against such claims that we infringe third- party patents or~~ **our** ~~violate other~~ intellectual property rights **, including enforcing** and ~~the outcome of such litigation~~ **defending intellectual property related claims** ; ~~● the timing, receipt~~ and ~~amount~~ **• the costs** of **operating as a public company. We believe that** ~~potential future licensee fees, milestone payments, and sales of, or~~ **our available financial resources will enable us** ~~royalties on, our future products, if any; and ● the extent~~ to **fund our operating expense requirements through at least 12 months from the issuance date of our audited consolidated financial statements included elsewhere in this Annual Report. However, our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of** which ~~we~~ may ~~acquire~~ **be beyond** ~~or~~ **our** ~~invest in~~ **control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek** additional **funds sooner** ~~businesses, product candidates and technologies. 40 Any additional fundraising efforts will divert certain members of our management team from their day- to- day activities, which may adversely affect our ability to develop our product candidates. We cannot guarantee that~~ **than planned** ~~future financing will be available in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all~~ . The terms of any future financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. ~~The~~ **For example, the** sale of additional equity securities and the conversion, exchange or exercise of certain of our outstanding securities will dilute all of our stockholders. The incurrence of debt could result in increased fixed payment obligations, and we could be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We may also seek funds through arrangements with collaborative partners in certain territories, including the U. S., or at an earlier stage than otherwise would be desirable or aligned with our business plan, and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. When necessary, if we are unable to obtain additional funding on a timely basis and on acceptable terms, we may be required to significantly curtail, delay or ~~discontinue~~ **terminate** one or more of our research or product development programs **, our pre- commercialization efforts** or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. **Due to the significant resources required for the development of our pipeline, and depending on our ability to access capital, we must prioritize the development of certain product candidates over others. Moreover, we may fail to expend our limited resources on product candidates or indications that may have been more profitable or for which there is a greater likelihood of success. Currently, we are developing or have development plans in place for six clinical- stage product candidates. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between aggressively pursuing our most advanced product candidates and indications and ensuring the development of additional potential product candidates and indications, on our own or with strategic collaborators. Due to the significant resources required for the development of our product candidates, we must decide which product candidates and indications to pursue and advance and the amount of resources to allocate to each.** Our **decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates, therapeutic areas or indications may not lead to the development of viable commercial products and may divert resources away from better opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the pharmaceutical industry, in particular for psychiatric and neurological disorders, our business, financial condition and results of operations could be materially and adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other disorders that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our** future ~~success is highly dependent upon~~ **cash needs through public or private equity offerings, debt financings, royalty- based financing, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations,**

even if we believe that we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interest of our stockholders may be diluted, and the terms of these securities could include liquidation or other preferences and anti- dilution protections that could adversely affect the rights of our common stockholders. In addition, royalty- based financing or debt financing, if available, may result in our relinquishing rights to valuable future revenue streams or fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to ~~successfully~~ **take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management team and may divert a disproportionate amount of our attention away from day- to- day activities, which may adversely affect our management team' s ability to oversee the development of our product candidates. If we raise additional capital through collaborations, strategic alliances or marketing, distribution or licensing arrangements, or royalty- based financings with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts, grant rights to** develop **and market product candidates that we would otherwise prefer to develop and market ourselves** ~~, on our own or~~ **obtain capital through arrangement** with collaborators ~~, any of~~ **on terms unfavorable to us** ~~our~~ **or** ~~current CNS~~ **pursue other strategies, all of which could adversely affect the holdings or the rights of our stockholders. Risks Related to** ~~product~~ **Product Development** ~~candidates or acquire or license additional CNS product candidates~~ **, Regulatory Approval The regulatory approval processes of the FDA** and **comparable foreign authorities are lengthy, time- consuming** ~~we cannot provide any assurance that we will successfully develop~~ and **inherently unpredictable, and if we are ultimately unable to** obtain regulatory approval ~~of~~ **for our product candidates, our business will be substantially harmed. We are not permitted to commercialize, market, promote or sell** any **product candidate in the U. S. without obtaining regulatory approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign authorities is inherently unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities and such factors may vary among jurisdictions. For instance, jurisdictions outside of the U. S., such as China, the European Union (EU) or Japan, may have different requirements for regulatory approval, which may require us to conduct additional clinical, nonclinical or chemistry, manufacturing and control studies. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development. To date, we have not submitted an NDA to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. We must complete additional preclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to seek or obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our initial and potential additional product candidates is susceptible to the risk of failure inherent at any stage of development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if any of our product candidates have a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of such product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of, or intolerability caused by, such product candidate, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case. Serious adverse events or other adverse events, as well as tolerability issues, could hinder or prevent market acceptance of the product candidate at issue. This lengthy approval process, as well as the unpredictability of clinical trial results, may result in our failing to obtain regulatory approval to market any product candidate we develop, which would substantially harm our business, results of operations and prospects. The FDA and other comparable foreign authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be granted for any product candidate that we develop. Even if we believe the data collected from future clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or any other regulatory authority. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post- marketing clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates. The FDA or comparable foreign regulatory authorities may disagree with our regulatory plan for our product candidates. In order to obtain FDA approval of our product candidates, we must, among other things, demonstrate substantial evidence of the effectiveness of such product candidates. FDA has generally considered this demonstration to require data gathered from two or more adequate and well- controlled**

clinical trials of the product candidate in the relevant patient population, or in some cases, one adequate and well-controlled trial plus other confirmatory evidence. Adequate and well- controlled clinical trials typically involve a large number of patients, have significant costs and take years to complete. The FDA or other regulatory authorities may disagree with us about whether a clinical trial is adequate and well- controlled or may request that we conduct additional clinical trials prior to granting any regulatory approval. In addition, there is no assurance that the doses, endpoints and trial designs that we intend to use for our ongoing and / or future clinical trials, including trials developed based on feedback from the FDA or other regulatory agencies or those that have been used for the approval of similar drugs, will be acceptable for future approvals. For example, while we have designed our registration- directed Phase 3 program for fasedienol after receiving input and feedback from the FDA, there can be no assurance that the design of our planned clinical trials will be satisfactory to the FDA or that the FDA will not require us to modify our trials or conduct additional testing, or that completing these trials will result in regulatory approval. Even if our ongoing and / or future clinical trials achieve their primary efficacy endpoint, there can be no assurance that the FDA will find them sufficient to support approval. Moreover, there are limited precedents for trial design, trial endpoints and regulatory pathway for certain therapeutic indications we are pursuing through the development of our product candidates, which may make clinical development and regulatory approval for those product candidates more challenging. Our clinical trial results may not support approval of our product candidates. In addition, our product candidates could fail to receive regulatory approval, or regulatory approval could be delayed, for many reasons, including the following: • the FDA or comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials; • the FDA or comparable foreign regulatory authorities may not file or accept our NDA or marketing application for substantive review; • the FDA or comparable foreign regulatory authorities may disagree with the dosing regimen, design or implementation of our clinical trials; • we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications; • the results of our clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; • we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks; • the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from our preclinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the U. S. or elsewhere; • the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. We are dependent on third parties having accurately generated, collected, interpreted and reported data from certain preclinical studies and clinical trials that were previously conducted for our product candidates. We have acquired substantially all of our current ~~CNS~~ product candidates **from Pherin as a result of the Pherin Acquisition,** ~~or~~ **for which Pherin undertook research and development prior to our acquisition or license. We had no involvement with or control over the preclinical and clinical development of our product candidates prior to acquiring or licensing them from Pherin. Therefore, we are dependent, in part, on Pherin' s prior research and development efforts in accordance with the applicable protocols, legal and regulatory requirements, and scientific standards utilized by them; having accurately reported the results of all preclinical studies and clinical trials conducted with respect to such product candidates and having correctly collected and interpreted the data from these studies and trials. These risks also apply to any additional product candidates that we may acquire or in- license in the** future ~~product candidates~~ **. If these activities were not compliant** , **accurate** ~~or that, if approved, any of our~~ **or** ~~CNS~~ **correct, the clinical development, regulatory approval or commercialization of our** product candidates will be **adversely affected** ~~successfully commercialized. Business development and research and development programs designed to identify, acquire or license additional product candidates require substantial technical, financial and human resources, whether or not any additional CNS product candidate is acquired or licensed~~ . If ~~beneficial, we may seek to collaborate with others to develop and commercialize any of our current or~~ **our clinical trials fail to replicate results from earlier preclinical studies or clinical trials conducted by us or** ~~future CNS product candidates, if and when they are acquired and developed. If we enter into arrangements with~~ third parties ~~to perform sales~~ , ~~marketing and distribution services~~ **we may be unable to successfully develop, obtain regulatory approval** for ~~our~~ **or commercialize our** ~~products~~ **product** ~~, the~~ **candidates. The** ~~resulting~~ **results observed** ~~revenues or the profitability~~ from ~~these revenues to us are likely to~~ **preclinical studies or early- stage clinical trials of our product candidates may not necessarily** be ~~lower~~ **predictive of the results of later- stage clinical trials** ~~than~~ **that** ~~if~~ we ~~had sold~~ **conduct. Similarly** , ~~marketed and distributed~~ **positive results from such preclinical studies** ~~our~~ **or clinical trials may not be replicated in our subsequent preclinical studies or clinical trials. Furthermore, our** ~~products~~ **product** ~~ourselves~~ **candidates may not be able to demonstrate similar activity or adverse event profiles as other product candidates that we believe may have similar profiles** . In addition, **in our planned future clinical trials,** we may **utilize clinical trial designs or dosing regimens that have** not **been tested in prior clinical trials. There can be no assurance that any of our clinical trials will ultimately** be successful ~~entering into arrangements with third parties to sell, market and distribute our~~ **or** ~~CNS~~ **support further clinical development of any of our** product candidates ~~or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. Risks Related to Product~~

~~Development, Regulatory Approval Failures of our current and / or future clinical studies of our product candidates could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business. Our PALISADE- 1 Phase 3 clinical study of fasedienol for the acute treatment of anxiety in adults with SAD did not achieve its primary endpoint, as measured by change from baseline using the SUDS as compared to placebo. Successful completion of our nonclinical and clinical trials is a prerequisite to submitting an NDA and, consequently, the ultimate approval required before commercial marketing of any product candidate we may develop. Failure of any of our current and / or future clinical and nonclinical trials to achieve the planned endpoints~~ , such as **the failure of** our PALISADE- 1 Phase 3 clinical trial of fasedienol **to meet its primary endpoint. There is a high failure rate for drugs proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials after achieving positive results in early- stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. To obtain the requisite regulatory approvals to commercialize any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. We may experience delays in completing our clinical trials or preclinical studies and initiating or completing additional clinical trials or preclinical studies, including as a result of regulators not allowing or delay in allowing clinical trials to proceed under an IND, or not approving or delaying approval for any clinical trial grant or similar approval we need to initiate a clinical trial. We may also experience numerous unforeseen events during our clinical trials that could delay or prevent our ability to receive marketing approval or commercialize the product candidates we develop, including: • regulators, IRBs, or other reviewing bodies such as ethics committees may not authorize us or our investigators to commence a clinical trial, or to conduct or continue a clinical trial at a prospective or specific trial site; • we may not reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • we may experience challenges or delays in recruiting principal investigators or study sites to lead our clinical trials; • the number of subjects or patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, and the number of clinical trials being conducted at any given time may be high and result in fewer available patients for any given clinical trial, or patients may drop out of these clinical trials at a higher rate than we anticipate; • our third- party contractors, including CMOs, CROs or other third- parties acting on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; • we may have to amend clinical trial protocols submitted to regulatory authorities or conduct additional studies to reflect changes in regulatory requirements or guidance, which may be required to resubmit to an IRB and regulatory authorities for re- examination; • regulators or other reviewing bodies may find deficiencies with, fail to approve or subsequently find fault with the manufacturing processes or facilities of third- party manufacturers with which we enter into agreements for clinical and commercial supplies, or the supply or quality of any product candidate or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and • the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval. Regulators or IRBs of the institutions in which clinical trials are being conducted may suspend, limit or terminate a clinical trial, or data monitoring committees may recommend that we suspend or terminate a clinical trial, due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Negative or inconclusive results from our clinical trials or preclinical studies could mandate repeated or additional clinical trials and, to the extent we choose to conduct clinical trials in other indications** , could result in **changes to or delays in clinical trials of our product candidates in such other indications. We do not know whether any clinical trials that we conduct will demonstrate efficacy and safety results adequate to obtain regulatory approval to market our product candidates for the indications that we are pursuing. If later- stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for our product candidates will be adversely impacted. Our failure to successfully initiate and complete clinical trials and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates would significantly harm our business. Our product candidate development costs will also increase if we experience delays in testing or regulatory approvals and we may be required to obtain additional funds to complete clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure or otherwise modify our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates. Business interruptions resulting from the COVID- 19 pandemic, the post- COVID environment and other public health crises could disrupt the development of our product candidates and adversely impact our business. Public health crises such as pandemics or similar outbreaks**

could adversely impact our business. For instance, the COVID- 19 pandemic and the post- COVID environment, including supply chain, labor market and other disruptions, as well as volatility in the global financial markets, in each case, driven by the pandemic, have impacted and may further impact our clinical trials or preclinical studies. In addition, COVID- 19, the post- COVID environment or future public health crises may impact our ability to retain principal investigators and site staff for our clinical trials. For instance, healthcare providers may have heightened exposure to COVID- 19 or may be impacted due to prioritization of hospital resources toward the pandemic and restrictions on travel. Our clinical trial sites may be located in geographies that are disproportionately affected by the COVID- 19 pandemic or actions taken by governmental and health authorities to address the pandemic. Furthermore, as a result of supply chain, labor market and other disruptions driven by the pandemic and the post- COVID environment, COVID- 19 has impacted and may further negatively affect our operations or the operations of our vendors, suppliers and business partners, including the third- party CROs, clinical sites and other vendors that we rely upon to carry out our clinical trials or the operations of our third- party manufacturers and other suppliers, which could result in delays or disruptions in the supply of our product candidates. The negative impact COVID- 19 or the post- COVID environment has on patient enrollment, site staffing or treatment or the timing and execution of our clinical trials has caused and could cause further delays to our clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our business and financial results. COVID- 19 and the post- COVID environment have also caused volatility in the global financial markets, including inflationary headwinds, which may negatively affect our ability to raise additional capital on attractive terms or at all. The extent to which COVID- 19 and the post- COVID environment impact our business, results of operations and financial condition will depend on future developments, including new variants or subvariants, which may impact rates of infection and the extent and effectiveness of actions to contain COVID- 19 or treat its impact, including vaccination campaigns, COVID- 19 treatments and lockdown measures, among others. In addition, recurrences or additional waves of COVID- 19 cases could cause other widespread or more severe impacts depending on where infection rates are highest. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if we or any of the third parties with whom we engage were to experience prolonged business shutdowns or other disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, results of operations and financial condition. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with our protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. Patient enrollment is affected by many factors, including: • the effects of the COVID- 19 pandemic and the post- COVID environment on our ability to recruit and retain patients; • the patient eligibility criteria defined in the protocol; • the size and nature of the patient population required for analysis of the trial' s primary endpoints; • the severity of the disease or condition under investigation; • the proximity of patients to study sites; • the design of the trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any drugs that may be approved for the indications that we are investigating; • patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; • our ability to obtain and maintain patient consents; and • the risk that patients enrolled in our clinical trials will drop out of the trials before completion. We may also experience challenges in recruiting principal investigators and patients to participate in ongoing and future clinical trials for our product candidates if we are unable to sufficiently demonstrate the potential of such product candidates to them. In addition, our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we may conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Furthermore, if significant adverse events or other side effects are observed in any of our clinical trials, we may have difficulty recruiting patients to our trials and patients may drop out of our trials. Finally, business disruptions, including those relating to natural disasters (including as a result of climate change), geopolitical incidents or macroeconomic conditions, may disrupt our clinical trials. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials or our development efforts altogether. Delays in patient enrollment may result in increased costs **, affect the timing or outcome of the planned clinical trials, product candidate development and approval process and jeopardize our ability** to ~~us~~ **seek and obtain the regulatory approval required to commence product sales and generate revenue, which could prevent completion of these trials, adversely affect our ability to advance the development of our product candidates, cause the value of the company to decline and limit our ability to obtain additional financing if needed. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates proceed through preclinical studies to late- stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as the vendors used to manufacture drug product or manufacturing methods and formulation, are altered along the way in** ~~and~~ **an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of**

these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA or comparable foreign regulatory authorities notification or approval. This could delay ~~,~~ or prevent completion of clinical trials, require conducting bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay or prevent approval of ~~or~~ our ~~limit~~ product candidates and jeopardize our ability to commence sales and generate revenue . Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time- consuming and uncertain and may prevent us from obtaining approvals for the commercialization of our product candidates. Any product candidate we develop and the activities associated with its development and commercialization, including its design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the U. S. and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of the product candidates we are developing or may seek to develop in the future will ever obtain regulatory approval. We have no experience in submitting and supporting the applications necessary to gain marketing approvals and expect to rely on third- party CROs or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate' s safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude its obtaining marketing approval or prevent or limit commercial use. The process of obtaining marketing approvals, both in the U. S. and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of ~~and~~ an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval that we may ultimately obtain could be limited or subject to restrictions or post- approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired. Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publish or publicly disclose interim, topline or preliminary data from our clinical trials. These publications or disclosures are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline, or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment ~~continue~~ continues and more patient data become available. Preliminary ~~our~~ or topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation and business prospects . ~~41~~ Further, disclosure of such data by us or by our competitors could result in volatility in the price of our common stock. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the development and commercialization of our product candidates may be delayed, and our business and results of operations may be harmed. For planning purposes, we sometimes estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, receipt of marketing approval or a commercial launch of a product. The achievement of many of these milestones may be

outside of our control. All of these milestones are based on a variety of assumptions which, if not realized as expected, may cause the timing of achievement of the milestones to vary considerably from our estimates, including: • our available capital resources or capital constraints we experience; • the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators; • our ability to identify, enroll and randomize patients who meet clinical trial eligibility criteria; • our receipt of approvals by the FDA and other regulatory authorities and the timing thereof; • other actions, decisions or rules issued by regulators; • our ability to access sufficient, reliable and affordable supplies of materials used to manufacture our product candidates; • the efforts of our collaborators with respect to the development and commercialization of our product candidates; and • the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities. If we fail to achieve announced milestones in the timeframes we expect, the development and commercialization of our product candidates may be delayed, and our business and results of operations may be harmed. We depend heavily on the success of one or more of our current ~~CNS~~ drug candidates and we cannot be certain that we will be able to obtain regulatory approval for any of our product candidates. We ~~currently have no drug products for sale and may never be able to develop marketable drug products. Our business currently depends heavily on the successful development, manufacturing and regulatory approval of one or more of our current CNS drug candidates, as well as our ability to acquire, license or produce and develop additional product candidates. Each of our current investigational CNS drug candidates will require substantial additional nonclinical and clinical development, manufacturing and regulatory approval before any of them may be commercialized, and there can be no assurance that any of them will ever achieve regulatory approval. The nonclinical and clinical development of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U. S. and in other countries where we or our collaborators intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through numerous nonclinical and clinical studies that the product candidate is safe and effective for use in each target indication. Research and development of product candidates in the pharmaceutical industry is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of nonclinical or clinical studies. This process takes many years and may also include post- marketing studies, surveillance obligations and drug safety programs, which would require the expenditure of substantial resources beyond the proceeds we have raised to date. Of the large number of drug candidates in development in the U. S., only a small percentage will successfully complete the required FDA regulatory approval process and will be commercialized. Accordingly, we cannot assure you that any of our current drug candidates or any future product candidates will be successfully developed or commercialized in the U. S. or any market outside the U. S. We~~ are not permitted to market our product candidates in the U. S. until we receive approval of **an** ~~a New Drug Application (~~NDA ~~)~~ from the FDA, or in any foreign countries until we receive the requisite approval from such countries. Obtaining FDA approval of ~~a~~ **an** NDA is a complex, lengthy, expensive and uncertain process. The FDA may refuse to permit the filing of our NDA, delay, limit or deny approval of ~~a~~ **an** NDA for many reasons, including, among others: ~~•~~ • if we submit an NDA and it is reviewed by a FDA advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional nonclinical or clinical studies, limitations on approved labeling or distribution and use restrictions; ~~•~~ ~~a~~ • **an** FDA advisory committee may recommend, or the FDA may require, a Risk Evaluation and Mitigation Strategies (REMS) safety program as a condition of approval or post- approval; ~~•~~ ~~a~~ • **an** FDA advisory committee or the FDA or applicable regulatory agency may determine that there is insufficient evidence of overall effectiveness or safety in ~~a~~ **an** NDA and require additional clinical studies; ~~•~~ • the FDA or the applicable foreign regulatory agency may determine that the manufacturing processes or facilities of third- party contract manufacturers with which we contract do not conform to applicable requirements, including ~~current Good Manufacturing Practices (~~cGMPs ~~)~~; or ~~•~~ • the FDA or applicable foreign regulatory agency may change its approval policies or adopt new regulations. Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for any current or future drug product candidate we may develop. Any such setback in our pursuit of regulatory approval for any product candidate would have a material adverse effect on our business and prospects. In addition, ~~certain of~~ our **pherine** product candidates, including fasedienol and itruvone, will be subject to regulation as combination products, which means that they are composed of both a drug product and device product. Although we do not contemplate doing so, if marketed individually, each component would be subject to different regulatory pathways and reviewed by different centers within the FDA. Our product candidates that are considered to be drug- device combination products will require review and coordination by FDA' s drug and device centers prior to approval, which may delay approval. In the U. S., a combination product with a drug primary mode of action generally would be reviewed and approved pursuant to the drug approval processes under the Federal Food, Drug and Cosmetic Act of 1938. In reviewing the NDA application for such a product, however, FDA reviewers in the drug center could consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. Under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality System ~~(QS)~~ regulations applicable to medical devices. Problems associated with the device component of the combination product candidate may delay or prevent approval. **Our** ~~42 The COVID- 19 pandemic has adversely impacted and may continue to adversely impact our business. Beginning in late- 2019, a new strain of coronavirus (COVID- 19) spread across the world and caused considerable uncertainty about the potential effects of the virus and its variants, and the extent of and effectiveness of responses taken on international, national and local levels. Measures taken to limit the impact of the pandemic, including shelter- in- place orders, social distancing measures, travel bans and restrictions, and business and government shutdowns, resulted in significant negative economic impacts on a global basis. The COVID- 19~~

pandemic has impacted our business and may continue to do so. Additionally, future outbreaks may have several adverse effects on our business, results of operations and financial condition. ● Adverse impact on product **candidates** development: Recent medical literature has reported that the SARS- COV- 2 virus, which causes COVID- 19, may cause long- term and reversible olfactory dysfunction (OD) in approximately 30 % of affected individuals. OD may occur in cases where the SARS- COV- 2 virus damages the nasal chemosensory epithelium, a structure in the nose where the types of cells are found that respond to pherines such as fasedienol, itruvone, PH15, PH80 and PH284. Accordingly, there is a risk that the prevalence of OD caused by COVID- 19 infections may interfere with the ability of our pherine nasal sprays to provide a therapeutic benefit, which, may, in turn, have a materially adverse impact on results of our clinical trials designed to assess the efficacy of these product candidates or a negative impact on potential future sales should any of our pherine nasal sprays be approved for commercialization. ● Negative impacts on our employees, collaborators and suppliers: COVID- 19 has impacted, and variant and subvariant strains of COVID- 19 or another highly transmissible and pathogenic infectious disease may impact or continue to impact, the health of our employees, collaborators, contractors or suppliers, reduce the availability of our workforce or those of companies with which we do business, divert our attention toward succession planning, or create disruptions in our supply or distribution networks. Since the beginning of the COVID- 19 pandemic, we have experienced delays of the delivery of supplies of active pharmaceutical product (API) required to continue development of fasedienol and itruvone. Although our supply of raw materials and API remains sufficiently operational, we may experience adverse effects of such events, which may result in a significant, material disruption to clinical development programs and our operations. Additionally, having substantially shifted to remote working arrangements, we also face a heightened risk of cybersecurity attacks or data security incidents and are more dependent on internet and telecommunications access and capabilities. COVID- 19 also created significant disruption and volatility in national, regional and local economies and markets. Uncertainties related to, and perceived or experienced negative effects from COVID- 19, may cause significant volatility or decline in the trading price of our securities, capital markets conditions and general economic conditions. Our future results of operations and liquidity could be adversely impacted by supply chain disruptions and operational challenges faced by our CROs, CMOs, clinical sites involved in our clinical studies and other contractors. The COVID- 19 pandemic, or another highly transmissible and pathogenic infectious disease, could result in a widespread health crisis that could adversely affect the economies and financial markets of many countries, resulting in a further economic downturn or a global recession. Such events may limit or restrict our ability to access capital on favorable terms, or at all, lead to consolidation that negatively impacts our business, weaken demand, increase competition, cause us to reduce our capital spend further, or otherwise disrupt our business or make it more difficult to implement our strategic plans. We have been granted Fast Track designation from the FDA for development of fasedienol for the treatment of social anxiety disorder (SAD) and AV- 101 for the adjunctive treatment of major depressive disorder (MDD) and for the treatment of neuropathic pain (NP). However, these designations may not actually lead to faster development or regulatory review or approval processes for fasedienol or AV- 101. Further, there is no guarantee the FDA will grant Fast Track designation for fasedienol or AV- 101 as a treatment option for other CNS indications or for any of our other product candidates in the future. The Fast Track designation is a program offered by the FDA, pursuant to certain mandates under the FDA Modernization Act of 1997, designed to facilitate drug development and to expedite the review of new drugs that are intended to treat serious or life- threatening conditions. Compounds selected must demonstrate the potential to address unmet medical needs. The FDA' s Fast Track designation allows for close and frequent interaction with the FDA. A designated Fast Track drug may also be considered for priority review with a shortened review time, rolling submission, and accelerated approval if applicable. The designation does not, however, guarantee FDA approval or expedited approval of any application for the product candidate. 43 In December 2017, the FDA granted Fast Track designation for development of AV- 101 for the adjunctive (add- on) treatment of MDD in patients with an inadequate response to current antidepressants. In September 2018, the FDA granted Fast Track designation for development of AV- 101 for the treatment of NP. In December 2019, the FDA granted Fast Track designation for development of fasedienol for the treatment of SAD. However, these FDA Fast Track designations may not lead to a faster development or regulatory review or approval process for fasedienol or AV- 101 and the FDA may withdraw Fast Track designation of fasedienol or AV- 101 if it believes that the respective designation is no longer supported by data from our clinical development programs. In addition, we may apply for Fast Track designation for fasedienol, AV- 101 and any of our other product candidates as a treatment option for other CNS indications. The FDA has broad discretion whether or not to grant a Fast Track designation, and even if we believe our product candidates may be eligible for this designation, we cannot be sure that the FDA will grant it. Results of earlier clinical trials may not be predictive of the results of later- stage clinical trials. The results of preclinical studies and early clinical trials of our current and / or our other future product candidates, if any, including positive results, may not be predictive of the results of later- stage clinical trials. Each of our current or any other future product candidates in later stages of clinical development may fail to show the desired safety and efficacy results despite having progressed through nonclinical studies and initial clinical trials, as is the case for results from our PALISADE- 1 clinical trial. Many companies in the biopharmaceutical industry have suffered significant setbacks in later- stage clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies. Similarly, our future clinical trial results may not be successful for these or other reasons. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in nonclinical studies and clinical trials nonetheless failed to obtain FDA approval or approval from a similar regulatory authority in another country. With respect to our current product candidates, if our future nonclinical or clinical studies fail to produce positive results, the development timeline and regulatory approval and commercialization prospects for these candidates and, correspondingly, our business and financial prospects, could be materially adversely affected. Any changes in planned timing or nature of clinical trials compared to completed clinical trials could impede our ability to meet our clinical development objectives for our product candidates. As product candidates are developed through preclinical to early- and late- stage clinical trials towards regulatory approval and

~~commercialization, it is customary that various aspects of the development program, such as manufacturing and methods of administration, are altered along the way in an effort to optimize processes and results. While these types of changes are common and are intended to optimize the product candidates for later stage clinical trials, approval and commercialization, such changes do carry the risk that they will not achieve these intended objectives. For example, the timing of planned clinical trials may be affected by delays caused by the ongoing COVID- 19 pandemic, including potential delays in recruitment and enrollment in our planned clinical and nonclinical studies or supply chain disruptions experienced by certain of our CMOs and / or CROs. In addition, clinical development of our products may be further affected if we or any of our collaborators seek to optimize and scale- up production of a product candidate. In such case, we will need to demonstrate comparability between the newly manufactured drug substance and / or drug product relative to the previously manufactured drug substance and / or drug product. Demonstrating comparability may cause us to incur additional costs or delay initiation or completion of our clinical trials, including the need to initiate a dose escalation study and, if unsuccessful, could require us to complete additional nonclinical or clinical studies of our product candidates. In addition, health and safety precautions at clinical sites related to the COVID- 19 pandemic could cause us to incur additional costs or delay initiation or completion of planned clinical and / or nonclinical trials. 44 If serious adverse events or other~~ undesirable side effects or **have** ~~safety concerns attributable to our product candidates occur, the~~ **other properties that could** ~~clinical development of our product candidates may be delayed --~~ **delay** or ~~adversely affected~~ **prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if obtained** . Undesirable side effects ~~or safety concerns~~ caused by **any of** our product candidates could cause us or regulatory authorities to interrupt, delay or halt ~~our~~ clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval **by the FDA or comparable foreign regulatory authorities** . **We may also observe safety or tolerability issues with** ~~Although no treatment- related serious adverse events (SAEs) were reported in any clinical trials of any of~~ our product candidates **in ongoing** ~~completed to date, if treatment- related SAEs or other undesirable side effects or safety concerns, or unexpected characteristics attributable to any of our --~~ **or** ~~product candidates are reported in any~~ future clinical trials **. Many compounds that initially showed promise in** ~~involving our drug candidates, they may adversely affect or delay our~~ clinical **or earlier- stage testing are later found to cause undesirable or unexpected side effects that prevented further** development ~~and commercialization~~ of ~~the effected product candidate, and the occurrence of these --~~ **the compound** ~~events could have a material adverse effect on our business and financial prospects~~ . Results of ~~our~~ future clinical trials **of our product candidates** could reveal a high and unacceptable severity and prevalence of ~~adverse~~ side effects **or unexpected characteristics, despite a favorable tolerability profile observed in earlier- stage testing** . ~~In such~~ **Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate** an ~~event~~ **apparent positive effect of a product candidate that is greater than the actual positive effect** , **if any, or alternatively fail to identify undesirable side effects. If unacceptable side effects arise in the development of our product candidates, we, the FDA or comparable foreign regulatory authorities, the IRBs, or independent ethics committees at the institutions in which** our trials **are conducted,** could ~~be suspended --~~ **suspend, limit** or ~~terminated --~~ **terminate our clinical trials** , ~~and~~ **or the independent safety monitoring committee could recommend that we suspend, limit or terminate our trials, or** the FDA or ~~other~~ **comparable foreign** regulatory ~~agency~~ **authorities** could order us to cease **clinical trials** ~~further development of~~ or deny approval of our product candidates for any or all targeted indications. ~~The~~ **Treatment- emergent side effects that are deemed to be** drug- related **could delay recruitment of clinical trial subjects or may cause subjects that enroll in our clinical trials to discontinue participation in our clinical trials. In addition, these** side effects **may not be appropriately recognized or managed by the treating medical staff. We may need to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates** could **result in harm to patients that are administered our product candidates. Any of these occurrences may adversely** affect ~~patient recruitment or~~ **our business, financial condition and prospects significantly** ~~the ability of enrolled patients to complete the trial or result in potential product liability claims~~ . Additionally, if any of our product candidates receives ~~marketing~~ **regulatory** approval **,** and we or others later identify undesirable ~~or unacceptable~~ side effects ~~or safety concerns~~ caused by ~~these~~ **such** product ~~candidates~~ , a number of potentially significant negative consequences could result **. For example** , **the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy (REMS), to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may** ~~including~~ **include , among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We may also be required to engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product. Other potentially significant negative consequences associated with adverse events include** : ~~● •~~ **we may be required to suspend marketing of a product, or we may decide to remove such product from the marketplace; •** regulatory authorities may withdraw ~~, suspend,~~ or ~~limit~~ **modify their** approvals of ~~such~~ **our** product ~~and require us to take them off the market~~ ; ~~• ● regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies; ● regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a REMS drug safety program or REMS- like plan to ensure that the benefits of the product outweigh its risks; ●~~ we may be required to ~~change the way a product is distributed or administered,~~ conduct ~~additional clinical trials or change the labeling of a product; ● we may be required to conduct additional~~ post- marketing studies ~~or surveillance~~ ; ~~● •~~ we may **be required to change the way our product is administered; • we could** be subject to **fines, injunctions, or** ~~limitations on how we may promote~~ the ~~product~~ **imposition of criminal or civil penalties,**

or be sued and held liable for harm caused to subjects or patients ; • ~~● sales of the product may decrease significantly; ● we may be subject to regulatory investigations, government enforcement actions, litigation or~~ **our** ~~product liability claims; and ● our products~~ -- **product** may become less competitive ~~or~~**, and •** our reputation may suffer. Any of these events could **diminish the usage or otherwise limit the commercial success of our product candidates and** prevent us ~~or any collaborators~~ from achieving or maintaining market acceptance of our product candidates ~~or could substantially increase commercialization costs and expense, which in turn could delay or prevent us from generating significant revenue from the sale of our product candidates. 45 Failures or delays in the commencement or completion of our planned nonclinical and clinical studies of our product candidates could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business. We will need to successfully complete at least two Phase 3 clinical trials and certain other clinical and nonclinical studies prior to our potential submission of an NDA for regulatory approval of fasedienol as an as needed, over time, treatment of anxiety in adults with SAD, or for any other anxiety disorder such as AjDA. For itruvone, at present, we believe we will need to complete at least one additional Phase 2B clinical study, two adequate and well- controlled Phase 3 clinical trials, as well as standard nonclinical and long- term clinical safety studies, as well as other smaller clinical studies prior to the potential submission of a NDA for regulatory approval of itruvone as a stand- alone rapid- onset treatment for MDD, or any other depression disorder. For AV- 101, we believe we will need to complete our ongoing exploratory Phase 1B clinical study, two Phase 2 clinical studies, two adequate and well- controlled Phase 3 clinical trials, additional toxicology and other standard nonclinical and long- term clinical safety studies, as well as certain standard smaller clinical studies prior to the potential submission of an NDA for regulatory approval in any CNS indication. For PH15, PH80 and PH284, we are in the process of determining the work required to sucessfuly complete the clinical and nonclinical development of each of these product candidates. Successful completion of our nonclinical and clinical trials is a prerequisite to submitting an NDA and, consequently, the ultimate approval required before commercial marketing of any product candidate we may develop. We do not know whether any of our future- planned nonclinical and clinical trials of any of our product candidates will be completed on schedule** , if ~~at all, as the commencement and completion of nonclinical and clinical trials can be delayed or prevented for a number of reasons, including, among others: ● the regulatory authority may deny permission to proceed with planned clinical trials or any other clinical trials we may initiate, or may place a planned or ongoing clinical trial on hold; ● delays in filing or receiving approvals from regulatory authorities of additional INDs that may be required; ● negative or ambiguous results from nonclinical or clinical studies; ● delays in reaching or failing to reach agreement on acceptable terms with prospective CROs, investigators and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs, investigators and clinical trial sites; ● delays in the manufacturing of, or insufficient supply of product candidates necessary to conduct nonclinical or clinical trials, including delays in the manufacturing of sufficient supply of drug substance or finished drug product; ● inability to manufacture or obtain clinical supplies of a product candidate meeting required quality standards; ● difficulties obtaining Institutional Review Board (IRB) approval to conduct a clinical trial at a prospective clinical site or sites; ● challenges in recruiting and enrolling patients to participate in clinical trials, including the proximity of patients to clinical trial sites; ● eligibility criteria for a clinical trial, the nature of a clinical trial protocol, the availability of~~ approved ~~effective treatments for the relevant disease and competition from other clinical trial programs for similar indications; ● severe or unexpected adverse drug- related side effects experienced~~ by ~~patients in a clinical trial; ● delays in validating any endpoints utilized in a clinical trial; ● the regulatory authority may disagree with our clinical trial design and our interpretation of data from prior nonclinical studies or clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials; ● reports from nonclinical or clinical testing of other~~ -- **the FDA** ~~CNS indications or therapies that raise safety or efficacy concerns; and ● difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trial, lack of efficacy, side effects, personal issues or loss of interest. 46 Clinical trials may also be delayed or terminated prior to completion as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the regulatory authority, the IRBs at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board (DSMB), overseeing the clinical trial at issue~~ or other regulatory authorities ~~due to a number of factors, including, among others: ● failure to conduct the clinical trial in accordance with regulatory requirements or approved clinical protocols; ● inspection of the clinical trial operations or trial sites by the regulatory authority that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold; ● unforeseen safety issues, including any that could be identified in nonclinical carcinogenicity studies, adverse side effects or lack of effectiveness; ● changes in government regulations or administrative actions; ● problems with clinical supply materials that may lead to regulatory actions; and ● lack of adequate funding to continue nonclinical or clinical studies. Changes in regulatory requirements, regulatory guidance or unanticipated events during our nonclinical studies and clinical trials of our CNS product candidates may occur, which may result in changes to nonclinical studies and clinical trial protocols or additional nonclinical studies and clinical trial requirements, which could result in increased costs to us and could delay our development timeline. Changes in regulatory requirements, guidance or unanticipated events during our nonclinical studies and clinical trials of any of our CNS product candidates may force us to amend nonclinical studies and clinical trial protocols or the regulatory authority may impose additional nonclinical studies and clinical trial requirements. Amendments or changes to our clinical trial protocols would require resubmission to the regulatory authority and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. Similarly, amendments to our nonclinical studies may adversely impact the cost, timing, or successful completion of those nonclinical studies. If we experience delays completing, or if we terminate, any of our nonclinical studies or clinical trials, or if we are required to conduct additional nonclinical studies or clinical trials, the commercial prospects for our CNS product candidates may be harmed and our ability to generate product revenue will be delayed. 47 We rely, and expect that we will continue to rely, on third parties to conduct our nonclinical and clinical trials of our current CNS product candidates and will continue to do so for any other future**

CNS product candidates. If these third parties do not successfully carry out their contractual duties and / or meet expected deadlines, completion of our nonclinical or clinical trials and development of our current and / or future CNS product candidates may be delayed and we may not be able to obtain regulatory approval for our current or future CNS product candidates and our business could be substantially harmed. By strategic design, we do not have the extensive internal staff resources to independently conduct nonclinical and clinical trials of our product candidates completely on our own. We rely on our network of strategic relationships with various academic research centers, medical institutions, nonclinical and clinical investigators, contract laboratories, CROs and other third parties to assist us to conduct and complete nonclinical and clinical trials of our product candidates. We enter into agreements with third- party CROs to provide monitors for and to manage data for our clinical trials, as well as provide other services necessary to prepare for, conduct and complete clinical trials. We rely heavily on these and other third parties for efficient execution of nonclinical and clinical trials for our product candidates and we control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these nonclinical and clinical trials and the management of data developed through nonclinical and clinical trials than would be the case if we were relying entirely upon our own internal staff resources. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties and inefficiencies in coordinating activities. CROs and other outside parties may: ● experience disruptions to their operations, such as staff attrition, reduced staffing and supply chain disruptions; ● have staffing difficulties and / or undertake obligations beyond their anticipated capabilities and resources; ● fail to comply with contractual obligations; ● experience regulatory compliance issues; ● undergo changes in priorities or become financially distressed; or ● form relationships with other entities, some of which may be our competitors. These factors may materially adversely affect the willingness or ability of third parties to conduct our nonclinical and clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our nonclinical studies and clinical trials is conducted and completed in accordance with the applicable protocol, legal, regulatory and scientific requirements and standards, and our reliance on CROs, or independent investigators does not relieve us of our regulatory responsibilities. We and our CROs, and any investigator in an investigator- sponsored study are required to comply with regulations and guidelines, including current Good Clinical Practice regulations (cGCPs) for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, any of our CROs or any of our third- party collaborators fail to comply with applicable cGCPs, the clinical data generated in clinical trials involving our product candidates may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with product candidates produced under cGMPs and will require a large number of test patients. Our failure or the failure of our CROs or other third- party collaborators to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties. Although we design our clinical trials for our product candidates, our clinical development strategy involves having CROs and other third- party investigators and medical institutions conduct clinical trials of our product candidates. As a result, many important aspects of our drug development programs are outside of our direct control. In addition, although CROs, or independent investigators or medical institutions, as the case may be, may not perform all of their obligations under arrangements with us or in compliance with applicable regulatory requirements, under certain circumstances, we may be responsible and subject to enforcement action that may include civil penalties up to and including criminal prosecution for any violations of FDA laws and regulations during the conduct of clinical trials of our product candidates. If such third parties do not perform clinical trials of our product candidates in a satisfactory manner, breach their obligations to us or fail to comply with applicable regulatory requirements, the development and commercialization of our product candidates may be delayed or our development program materially and irreversibly harmed. In certain cases, including investigator- sponsored clinical studies, we cannot control the amount and timing of resources these third parties devote to clinical trials involving our product candidates. If we are unable to rely on nonclinical and clinical data collected by our third- party collaborators, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures. 48 If our relationships with one or more of our third- party collaborators terminates, we may not be able to enter into arrangements with alternative third- party collaborators. If such third- party collaborators, including our CROs, do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to applicable clinical protocols, regulatory requirements or for other reasons, any clinical trials that such third- parties are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully develop and commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs would increase and our ability to generate revenue would be delayed. We rely completely on third parties to manufacture, formulate, analyze, hold and distribute supplies of our CNS product candidates for all nonclinical and clinical studies, and we intend to continue to rely on third parties to produce all nonclinical, clinical and commercial supplies of our CNS product candidates in the future. By strategic design, we do not currently have, nor do we plan to acquire or develop, extensive internal infrastructure or technical capabilities to manufacture, formulate, analyze, hold or distribute supplies of our product candidates, for use in nonclinical and clinical studies or commercial scale. As a result, with respect to all of our product candidates, we rely, and will continue to rely, completely on CMOs to manufacture API and

formulate, hold and distribute final drug product. The facilities used by our CMOs to manufacture API and formulate final drug product for any of pir product candidates are subject to a pre- approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable regulatory guidelines and requirements, including cGMPs, and may be required to undergo similar inspections by the FDA or other comparable foreign regulatory agencies, after we submit INDs, NDAs or relevant foreign regulatory submission equivalent to the applicable regulatory agency. We do not directly control the manufacturing process, or the supply or quality of materials used in the manufacturing, analysis and formulation of our product candidates, and, with respect to all of our product candidates, we are completely dependent on our CMOs to comply with all applicable cGMPs for the manufacturing of both API and finished drug product. If our CMOs cannot secure adequate supplies of suitable raw materials due to supply chain disruptions, or successfully manufacture our product candidates, including API and finished drug product, that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, production of sufficient supplies of our product candidates, including API and finished drug product, may be delayed and our CMOs may not be able to secure and / or maintain regulatory approval for their manufacturing facilities, or the FDA may take other actions, including the imposition of a clinical hold. In addition, we have no direct control over our CMOs' ability to maintain adequate quality control, quality assurance and qualified personnel. All of our CMOs are engaged with other companies to supply and / or manufacture materials or products for such other companies, which exposes our CMOs to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our CMO' s facilities generally or affect the timing of manufacture of any of our product candidates for required or planned nonclinical and / or clinical studies. If the FDA or an applicable foreign regulatory agency determines now or in the future that our CMOs' facilities are noncompliant, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market our product candidates. Our reliance on CMOs also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information. We do not yet have long- term supply agreements in place with our CMOs and each batch manufactured of our product candidates is or will be individually contracted under a separate supply agreement. If we engage new CMOs, such contractors must complete an inspection by the FDA and other applicable foreign regulatory agencies. We plan to continue to rely upon CMOs and, potentially, collaboration partners, to manufacture research and development scale, and, if approved, commercial quantities of our product candidates. Although we believe our current scale of API manufacturing for AV- 101, and our contemplated scale of API manufacturing for fasedienol, itruvone, PH15, PH80 and PH284, and the current and projected supply of API and finished drug product for each of our product candidates will be adequate to support our planned nonclinical and clinical studies, no assurance can be given that unanticipated supply shortages or CMO- related delays in the manufacture and formulation of API and / or finished drug product for any or all of our product candidates will not occur in the future. 49 Additionally, fasedienol, itruvone, PH15, PH80 and PH284 will be considered drug- device combination products. Third- party manufacturers may not be able to comply with cGMP requirements applicable to drug / device combination products, including applicable provisions of the FDA' s or a comparable foreign regulatory authority' s drug cGMP regulations, device cGMP requirements embodied in the Quality System Regulation (QSR) or similar regulatory requirements outside the U. S. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. The facilities used by our CMOs to manufacture our product candidates must be approved by the FDA and comparable foreign regulatory authorities pursuant to inspections that will or may be conducted after we submit our NDA. We do not control the manufacturing process of, and are completely dependent on, our CMO partners for compliance with cGMPs and QSRs. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other comparable foreign regulatory authorities, they will not be able to secure and / or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. CMOs may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP and QSR requirements. Any failure to comply with cGMP or QSR requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval. Even if we receive marketing approval for any of our CNS product candidate in the U. S., we may never receive regulatory approval to market the same CNS product candidate outside of the U. S. In order to market any of our CNS product candidate outside of the U. S., we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the U. S. as well as other risks. In particular, in many countries outside of the U. S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other

~~setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects~~ . If any of our ~~CNS~~ product candidates are ultimately regulated as controlled substances, we, our CMOs, as well as future distributors, prescribers, and dispensers will be required to comply with additional regulatory requirements which could delay the marketing of our product candidates, and increase the cost and burden of manufacturing, distributing, dispensing, and prescribing our product candidates. Before we can commercialize our product candidates in the U. S. or any market outside the U. S., the U. S. Drug Enforcement Administration (DEA) or its foreign counterpart may need to determine whether such product candidates will be considered to be a controlled substance, taking into account the recommendation of the FDA or its foreign counterpart, as the case may be. This may be a lengthy process that could delay our marketing of a product candidate and could potentially diminish any regulatory exclusivity periods for which we may be eligible, which would increase the cost associated with commercializing such products and, in turn, may have an adverse impact on our results of operations. Although we currently do not know whether the DEA or any foreign counterpart will consider any of our current or future product ~~candidate~~ **candidates** to be controlled substances, we cannot yet give any assurance that such product candidates will not be regulated as controlled substances. ~~50~~ If any of our product candidates are regulated as controlled substances, depending on the DEA controlled substance schedule in which the product candidates are placed or that of its foreign counterpart, we, our CMOs, and any future ~~distributers~~ **distributors** , prescribers, and dispensers of the scheduled product candidates may be subject to significant regulatory requirements, such as registration, security, recordkeeping, reporting, storage, distribution, importation, exportation, inventory, quota and other requirements administered by the DEA or a foreign counterpart of the DEA as the case may be. Moreover, if any of our product candidates are regulated as controlled substances, we and our CMOs would be subject to initial and periodic DEA inspection. If we or our CMOs are not able to obtain or maintain any necessary DEA registrations or comparable foreign registrations, we may not be able to commercialize any product candidates that are deemed to be controlled substances or we may need to find alternative CMOs, which would take time and cause us to incur additional costs, delaying or limit our commercialization efforts. Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates, should they be deemed to contain controlled substances. Failure to comply with the applicable controlled substance laws and regulations can also result in administrative, civil or criminal enforcement. The DEA or its foreign counterparts may seek civil penalties, refuse to renew necessary registrations, or initiate administrative proceedings to revoke those registrations. In some circumstances, violations could result in criminal proceedings or consent decrees. Individual states also independently regulate controlled substances. ~~If~~ **We have concentrated our research and development efforts on the treatment of psychiatric and neurological disorders, a field that faces certain challenges in drug development. We have focused our research and development efforts on addressing psychiatric and neurological disorders. Efforts by pharmaceutical companies in this field have faced certain challenges in drug development. In particular, many neuroscience disorders such as anxiety and depression disorders rely on subjective assessments by clinicians and subjective patient- reported outcomes as key endpoints. This makes them more difficult to evaluate than indications with more objective endpoints. Furthermore, these indications are often subject to a placebo effect, which may make it more challenging to isolate the beneficial effects of our product candidates. There can be no guarantee that we will successfully overcome these challenges with our product candidates or that we will not encounter other challenges in the development of our product candidates. Even if any of our product candidates receives regulatory approval, it may fail to achieve the degree of market acceptance by physicians, patients, third- party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable. We have never commercialized a product, and even if any of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to achieve sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. Certain of the indications for our product candidates have well- established standards of care that physicians, patients and payors are familiar with and, in some cases, are available generically. Even if our product candidates are successful in registrational clinical trials, they may not be successful in displacing these current standards of care, if any, if** we are unable to ~~establish broad sales~~ **demonstrate superior efficacy, safety, ease of administration** and **/ or cost- effectiveness. For example, physicians may be reluctant to take their patients off their current medications and switch their treatment regimen to our product candidates. Further, patients often acclimate to the treatment regimen that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch due to lack of coverage and adequate reimbursement. Even if we are able to demonstrate our product candidates' safety and efficacy to the FDA and other regulators, safety or efficacy concerns in the medical community may hinder** ~~marketing --- market capabilities~~ **acceptance. Efforts to educate the medical community and third- party payors** on ~~our own~~ **the benefits of** ~~or~~ **our** ~~enter into agreements with third parties to market and sell our CNS~~ product candidates **may require significant resources** , ~~we~~ **including management time and financial resources, and** may not be ~~able~~ **successful. For example, even if fasedienol ultimately receives regulatory approval, we may have difficulty in convincing the medical community that fasedienol has the potential** to **deliver promising therapeutic benefits above and beyond antidepressants. If any product candidate is approved but does not achieve an adequate level of market acceptance, we may not** generate ~~any~~ **significant** ~~revenue~~ **revenues** ~~from product sales. We currently have limited internal resources for the sale, marketing and distribution of pharmaceutical products,~~ and we may not **become profitable** ~~be able to create broad internal capabilities in the foreseeable future~~ . ~~Therefore, to~~ **The degree of** market **acceptance of** our ~~CNS~~ product candidates, if approved ~~by the FDA or any other regulatory body, we must establish broad internal capabilities related to sales, marketing, managerial and other non- technical capabilities relating to the commercialization of our product candidates or make contractual arrangements with third parties to perform such services, prior to market approval. If we are unable to establish adequate internal sales, marketing and distribution~~

capabilities, or if we are unable to do so contractually on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected. Moreover, creating broad sales and marketing capabilities will require substantial capital, which we may not be able to obtain. Even if we receive marketing approval for our CNS product candidates, our product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales. The commercial **sale** success of our CNS product candidates, if approved by the FDA or other regulatory authorities, will depend upon the awareness and acceptance of our product candidates among the medical community, including physicians, patients and healthcare payers. Market acceptance of our product candidates, if approved , will depend on a number of factors, including , among others : ● • the efficacy and safety of our product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for **product; •** the **potential advantages of the product** applicable indications, to provide patients with incremental health benefits, as compared **to competitive** with other available therapies; ● limitations **• the prevalence and severity of any side effects; • whether the product is designated under physician treatment guidelines as a first-, second- or third- line therapy; •** or **our** warnings contained in **ability, or** the labeling approved **ability of any future collaborators, to offer the product** for **sale at competitive prices** our product candidates by the FDA or other applicable regulatory authorities ; ● • the clinical indications for which our product **' s convenience** candidates are approved; ● availability of alternative treatments already approved or expected to be commercially launched in the near future; ● the potential and **ease** perceived advantages of **administration compared to** our product candidates over current treatment options or alternative treatments, including future alternative treatments; ● • the willingness of the target patient population to try **,** new therapies and of physicians to prescribe **,** these -- **the** therapies **product** ; ● • **limitations or warnings, including distribution or use restrictions contained in the product' s approved labeling; •** the strength of **sales,** marketing and distribution support and timing of market introduction of competitive products ; ● publicity concerning our **• changes in the standard of care for the targeted indications for the** products **product** or competing products and treatments ; 51 ● pricing and cost effectiveness; ● **• availability and adequacy of coverage and reimbursement from government payors, managed care plans and** the **other** effectiveness of our sales and marketing strategies; ● our ability to increase awareness of our product candidates through marketing efforts; ● our ability to obtain sufficient third- party coverage **payors. Any failure by one or more of** or **our** reimbursement; **product candidates that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect** or **our business prospects** ● the willingness of patients to pay out- of- pocket in the absence of third- party coverage . If **we fail to develop and commercialize other product candidates, we may be unable to grow** our CNS **business and our ability to achieve our strategic objectives would be impaired. Although the development and commercialization of our current** product candidates are approved but do not achieve **our initial focus, as part of our longer- term growth strategy, we plan to develop other product candidates. We intend to evaluate internal opportunities from our existing product candidates or other potential product candidates,** an **and** adequate level of acceptance **also may choose to in- license or acquire other product candidates to treat patients suffering from other disorders with significant unmet medical needs and limited treatment options. These other potential product candidates will require additional, time- consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval** by patients, physicians and payers, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payers may require us to demonstrate that our product candidates, in addition to treating these -- **the FDA** target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and **applicable foreign** third- party payers about the benefits of our product candidates may require significant resources and may never be successful. Our CNS product candidates may cause undesirable safety concerns and side effects that could delay or prevent their regulatory **authorities** approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any . **All** If our product candidates are determined **prone** to cause undesirable side effects and **the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently** safety -- **safe and effective** concerns, we or **for** regulatory authorities may interrupt, delay or halt nonclinical studies and clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by regulatory authorities. **In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives. In addition, we intend to devote substantial capital and resources for basic research to discover and identify additional pherine product candidates. These research programs require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential pherine product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following: • the research methodology used may not be successful in identifying potential product candidates; • competitors may develop alternatives that render our product candidates obsolete; • product candidates that we develop may nevertheless be covered by third parties' patents or other exclusive rights; • a product candidate may, on** Further **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 product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and • a product candidate may not be accepted as safe and effective by patients, the medical community or third- party payors. In the future, we may also seek to in- license or acquire product candidates or the underlying technology. The process of proposing, negotiating and implementing a license or acquisition is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates. We have limited resources to identify and execute the acquisition or in- licensing of third- party products, businesses and technologies and**

integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all. In addition, future acquisitions may entail numerous operational and financial risks, including: • exposure to unknown liabilities; • disruption of our business and diversion of management' s time and attention to develop acquired products or technologies; • incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions; • higher than expected acquisition and integration costs; • difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel; • increased amortization expenses; • impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and • inability to motivate key employees of any acquired businesses. If we are unsuccessful in identifying and developing additional product candidates, either through internal development or licensing or acquisition from third parties, our potential for growth and achieving our strategic objectives may be impaired. The number of patients with the neuroscience disorders for which we are developing our product candidates has not been established with precision. If the actual number of patients with the disorders we elect to pursue with our product candidates is smaller than we anticipate, we may have difficulties in enrolling patients in our clinical trials by , which may delay or prevent development of our product candidates. Even if such product candidates are successfully developed and approved, their -- the nature utilize markets for our products may be smaller than we expect and our revenue potential and ability to achieve profitability may be materially adversely affected. Our pipeline includes product candidates for a sample variety of potential neuroscience disorders. There is no precise method of establishing the actual number of patients with any of these disorders in any geography over any time period. With respect to many of the indications in which we have developed, are developing, or plan to develop our product candidates, we have estimates of the prevalence of the disease or disorder. Our estimates as to prevalence may not be accurate, and the actual prevalence or addressable patient populations - population . With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or for some others identify undesirable safety concerns or all of those indications, side effects caused by such product candidates (or any other similar indication that we elect to pursue, may be significantly smaller than our estimates. In estimating the potential prevalence of indications we are pursuing, or may in the future pursue, including our estimates as to the prevalence of SAD, MDD and vasomotor symptoms (hot flashes) due to menopause, we apply assumptions to available information that may not prove to be accurate. In each case, there is a range of estimates in the published literature and in marketing studies, which include estimates within the range that are lower than our estimates. The actual number of patients with these disease indications may, however, be significantly lower than we believe. Even if our prevalence estimates are correct, our product candidates may be developed for only a subset of patients with the relevant disease or disorder or our products), if approved, may be indicated for or used by only a subset. In the event the number of patients with the diseases and disorders we are studying is significantly lower than we expect, we may have difficulties in enrolling patients in our clinical trials, which may delay or prevent development of our product candidates. If any of our product candidates are approved and our prevalence estimates with respect to any indication or our other market assumptions are not accurate, the markets for our product candidates for these indications may be smaller than we anticipate, which could limit our revenues and our ability to achieve profitability or to meet our expectations with respect to revenues or profits. Competitive products may reduce or eliminate the commercial opportunity for our product candidates, if approved. If our competitors develop technologies or product candidates more rapidly than we do, or their technologies or product candidates are more effective or after - safer such approval than ours , our ability to develop and successfully commercialize our product candidates may be adversely affected. The clinical and commercial landscapes for the treatment of neuroscience disorders, including those we are pursuing, are highly competitive and subject to rapid and significant technological change. We face competition with respect to our indications for our product 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 potentially significant negative consequences could result, including: ● regulatory authorities may withdraw or limit are pursuing their -- the approval development of drug such product candidates ; ● regulatory authorities may require the addition of labeling statements, such as a " black box " warning or for a contraindication; ● we may be required to change the way such product candidates treatment of the indications that we are distributed or administered pursuing. Potential competitors also include academic institutions , government agencies and other public and private research organizations that conduct research, seek patent protection additional clinical trials or change the labeling of the product candidates; ● we may be subject to regulatory investigations and establish collaborative arrangements government enforcement actions; ● we may decide to remove such product candidates from the marketplace; ● we could be sued and held liable for research, development, manufacturing injury caused to individuals exposed to or taking our product candidates; and commercialization ● our reputation may suffer . We believe that any a significant number of product candidates are currently under development for certain of these -- the events could prevent us from same indications we are currently pursuing, and some or all may become commercially available in the future for the treatment of conditions for which we are trying or may try to develop product candidates. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. See the section entitled " Business — Competition " in this Annual Report for examples of the

competition that our product candidates face. In most cases, we do not currently plan to run head- to- head clinical trials evaluating our product candidates against the current standards of care, which may make it more challenging for our product candidates to compete against the current standards of care due to the lack of head- to- head clinical trial data. Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Accordingly, our competitors may be more successful than we may be in obtaining regulatory approval for therapies and achieving **widespread** ~~or maintaining~~ market acceptance **. Our competitors' products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our therapies obsolete or non- competitive before we can recover development and commercialization expenses. If any** of **our** ~~the affected~~ product candidates ~~and~~ **are approved, it** ~~would~~ **could** ~~substantially increase the costs~~ **compete with a range** of ~~commercializing~~ **therapeutic treatments that are in development. In addition, our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than** our product candidates **, which could render** ~~and significantly impact our ability to successfully commercialize~~ our product candidates **obsolete** and **noncompetitive** ~~generate revenues~~ . **If** ~~52 Even if~~ we **obtain** ~~receive marketing~~ approval for **any of** our ~~CNS~~ product candidates, we may ~~still~~ face **competition based on many different factors, including the efficacy, safety and tolerability of our products, the ease with which our products can be administered, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Existing and** future **competing products could present superior treatment alternatives, including being more effective, safer, less expensive or marketed and sold more effectively than any products we may** ~~development ---~~ **develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing** and **commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. In addition, our competitors may obtain patent protection,** regulatory ~~difficulties. Even if~~ **exclusivities or FDA approval and commercialize products more rapidly than** we **do, which may impact future approvals or sales of any of our product candidates that** receive ~~marketing~~ **regulatory** approval ~~for our CNS~~ **. If the FDA approves the commercial sale of any** product ~~candidates~~ **candidate** , **we** ~~regulatory authorities may still impose significant restrictions on our product candidates, indicated uses or marketing or impose ongoing requirements for potentially costly post- approval studies. Our product candidates~~ will also be ~~subject~~ **competing with respect** to ~~ongoing regulatory requirements governing the labeling, packaging, storage and promotion of the product and record keeping and submission of safety and other post- market information. The FDA and other regulatory authorities have significant post-~~ marketing **capabilities and manufacturing efficiency. We expect competition among products will be** ~~authority, including, for example, the authority to require labeling changes~~ based on ~~new~~ **product efficacy and** safety **,** ~~information and to require post- marketing studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA and other~~ **the timing** ~~regulatory authorities also have the authority to require, as part of an~~ **and scope** ~~NDA or post- approval, the submission of a REMS or comparable drug safety program. Any REMS or comparable drug safety program required by the FDA or other regulatory authority may lead to increased costs to assure compliance with new post- approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. Manufacturers of drug and device products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with our product candidates, such as adverse events of unanticipated severity or frequency, or problems with the facility where our product candidates are manufactured, a regulatory agency may impose restrictions on our product candidates, the manufacturer or us, including requiring withdrawal of our product candidates from the market or suspension of manufacturing. If we, our product candidates, or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things: ● issue warning letters or untitled letters; ● seek an injunction or impose civil or criminal penalties or monetary fines; ● suspend or withdraw marketing approval; ● suspend any ongoing clinical trials; ● refuse to approve pending applications or supplements to applications submitted by us; ● suspend or impose restrictions on operations, including costly new manufacturing requirements; or ● seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall. Competing therapies could emerge adversely affecting our opportunity to generate revenue from the sale of our CNS product candidates. The pharmaceutical industry is highly competitive. There are many public and private pharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of product candidates that may be similar to and compete with our product candidates or address similar markets. It is probable that the number of companies seeking to develop product candidates similar to and competitive with our product candidates will increase in the future. Currently, management is unaware of any FDA- approved rapid- onset, treatment of anxiety in adults with SAD having the same mechanism of pharmacological action and safety profile as fasedienol. Also, management is currently unaware of any FDA-approved oral treatment for MDD having the same mechanism of pharmacological action and safety profile as our intranasally-administered ituvone or our orally administered AV- 101 in combination with probenecid. However, new antidepressant products with other mechanisms of pharmacological action or products approved for other indications, including the FDA-approved anesthetic ketamine hydrochloride administered intravenously, are being or may be used for treatment of MDD, as well as other CNS indications for which ituvone or AV- 101 in combination with probenecid may have therapeutic potential. Additionally, other non- pharmaceutical treatment options, such psychotherapy and electroconvulsive therapy (ECT) are used before or instead of standard antidepressant medications to treat patients with MDD. 53 With respect to fasedienol and current treatment options for SAD in the U. S., our competition may include, but is not limited to, current generic oral antidepressants**

~~approved by the FDA for treatment of SAD, as well as certain classes of drugs prescribed on an off-~~ **of** ~~label basis for treatment of SAD, including benzodiazepines such as alprazolam, and beta blockers such as propranolol, and certain investigational oral drug candidates in Phase 2 development. In the field of new generation, oral treatments for adult patients with MDD, we believe our principal competitors may be Axsome, Alkermes, Relmada and Sage. Additional potential competitors may include, but not be limited to, academic and private commercial clinics providing intravenous ketamine therapy on an off- label basis and Janssen's intranasally- administered esketamine. We are still assessing our competition for PH80 for the treatment of hot flashes due to menopause and for migraine headaches, PH15 to improve cognitive impairment and PH284 for the loss of appetite. Many of our potential competitors, alone or with their collaborators, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development, obtaining FDA and other~~ regulatory approvals, **availability** ~~and the commercialization~~ of ~~investigational~~ **supply, marketing and sales capabilities, product price, reimbursement coverage by government and private third- party payors, regulatory exclusivities and patent position. Our profitability and financial position will suffer if our** product candidates **receive regulatory** ~~. With respect to fasedienol, in addition to potential competition from certain current FDA- approved~~ **approval** ~~antidepressants and off- label use of benzodiazepines and beta blockers, we believe additional drug candidates in development for SAD may include,~~ but ~~potentially not be limited to,~~ **cannot compete effectively in the marketplace. Mergers** ~~an~~ **and acquisitions** ~~oral fatty acid amide hydrolase inhibitor~~ in ~~development by Janssen, and two oral drug candidates in Phase 2 development that act on the alpha- 7 nicotinic acetylcholine receptor, one in development by Bionomies and the other~~ -- **the** ~~in development by Vanda. With respect to itruvone and AV- 101 in combination with probenecid for treatment of depression disorders, including MDD, and AV- 101 in combination with probenecid for treatment of certain neurological disorders, including levodopa- induced dyskinesia associated with therapy for Parkinson's disease, neuropathic pain, and epilepsy, we believe a range of~~ pharmaceutical and biotechnology ~~companies have programs to develop new drug candidates and / or medical device technologies for such indications, including, but not limited to, Abbott Laboratories, Acadia, Allergan, Alkermes, Aptynix, AstraZeneca, Axsome, Eli Lilly, GlaxoSmithKline, IntraCellular, Janssen, Lundbeck, Merck, Neurocrine, Novartis, Ono, Otsuka, Pfizer, Relmada, Roche, Sage, Sumitomo Dainippon, Takeda and Xenon, as well as any affiliates of the foregoing companies. Mergers and acquisitions in the biotechnology and pharmaceutical~~ 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 and management personnel and establishing clinical trial sites, as well as in acquiring technologies complementary to, or necessary for, our programs. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates. We currently have no marketing, sales or distribution capabilities. We intend to establish a sales and marketing organization, either on our own or in collaboration with third parties, with technical expertise and supporting distribution capabilities to commercialize one or more of our product candidates that may receive regulatory approval in key territories. These efforts will require substantial additional resources, some or all of which may be incurred in advance of any approval of the product candidate. Any failure or delay in the development of our or third parties' internal sales, marketing and distribution capabilities would adversely impact the commercialization of our product candidates. Factors that may inhibit our efforts to commercialize our product candidates on our own include: • our inability to recruit and retain adequate numbers of effective sales and marketing leadership and sales personnel; • the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and • unforeseen costs and expenses associated with creating an independent sales and marketing organization. With respect to our existing and future product candidates, we may choose to collaborate with third parties that have direct sales forces and established distribution systems to serve as an alternative to our own sales force and distribution systems.** Our **future product revenue may be lower than if we directly marketed or sold our product candidates, if approved. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third parties, which may not be successful and are generally not within our control. If we are not successful in commercializing any approved products, our future product revenue will suffer and we may incur significant additional losses. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. Product liability lawsuits against us or any of our future collaborators could divert our resources and attention, cause us to incur substantial liabilities and limit commercialization of our product candidates. We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. Currently, we have no products that have been approved for** commercial ~~opportunity~~ **sale; however, the use of our product candidates by us and any collaborators in clinical trials, and the sale of these product candidates, if approved, in the future, may expose us to liability claims. We face an inherent risk of product liability lawsuits related to the use of our product candidates in patients and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us by participants enrolled in our clinical trials, patients, health care providers, pharmaceutical companies, our collaborators or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for any of our future approved products; • injury to our reputation; • withdrawal of clinical trial participants; • termination of clinical trial**

sites or entire trial programs; • significant litigation costs; • substantial monetary awards to, or costly settlements with, patients or other claimants; • product recalls or a change in the indications for which they may be used; • loss of revenue; • diversion of management and scientific resources from our business operations; and • the inability to commercialize our product candidates. Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be **adversely affected** ~~reduced or eliminated~~ if **we are subject to negative publicity associated with illness** ~~our~~ **or** ~~competitors develop and~~ **other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies. Although we maintain product liability insurance coverage consistent with industry norms, including clinical trial liability, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we** commercialize **any** ~~products~~ **product that receives regulatory approval. Insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects. Cyberattacks or other failures in our telecommunications or information technology systems, or those of our collaborators, CROs, third- party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations. We, along with our collaborators, CROs, third- party logistics providers, distributors and other contractors and consultants, utilize information technology (IT) systems and networks to process, transmit and store electronic information, including confidential information such as proprietary business information and personal information of our employees and contractors, in connection with our business activities. As use of digital technologies has increased, our IT systems and those of our third- party service providers, strategic partners and other contractors or consultants are increasingly vulnerable to attack, damage and interruption from cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, computer malware (e. g., ransomware), viruses, malicious code, spamming, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation- state and nation- state- supported actors, natural disasters, terrorism, war, telecommunication and electrical failures or other threats. Deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our, our collaborators', CROs', third- party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. We may not be successful in preventing or identifying cyberattacks and may experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or successfully mitigate their effects due to attackers increasingly using tools and techniques** that are ~~safer~~ **designed to circumvent controls** , ~~more effective~~ **to avoid detection** , **and to remove or obfuscate forensic evidence. Like other companies, we** have ~~fewer~~ **on occasion experienced, and will continue to experience, threats to** ~~or~~ **our data and systems, including malicious codes and viruses, phishing, business email compromise attacks or other cyberattacks. Similarly, our collaborators, CROs, third- party logistics providers, distributors and other contractors and consultants may not be successful in protecting our clinical and other data that is stored on their systems. Any cyberattack, data breach or destruction or** ~~less~~ **loss** ~~severe side effects~~ **of data could result in a violation of applicable U. S. and international privacy** , **data protection and other laws and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the U. S. and by international regulatory entities, resulting in exposure to material civil and / or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we** are ~~more convenient~~ **exposed and may not be adequate to indemnify us** ~~or~~ **for all liability** ~~are less expensive than~~ **that may be imposed, which could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed or ongoing clinical trials for** any **of our** ~~products~~ **product candidates could result in delays in** ~~that we may develop. Our competitors also may obtain FDA or~~ **our** ~~other~~ **development and** regulatory approval **efforts and significantly increase** ~~for their products more rapidly than we may obtain approval for ours~~ **our costs to recover or reproduce the data. In addition** , ~~which could~~ **we may suffer reputational harm or face litigation or adverse regulatory action as a** result ~~in of cyberattacks~~ ~~our~~ **or** ~~competitors establishing a strong market position before we are able to enter the~~ **other** ~~market~~ **data security breaches and may incur significant additional expense to implement further data protection measures** . We may seek to establish collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans. Our drug development programs and the potential commercialization of our ~~investigational~~ product candidates will require substantial additional cash to fund expenses. We may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates ~~, such as the AffaMed Agreement~~ . We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter ~~,~~ ~~including the AffaMed Agreement~~ . However, our ability to generate revenue from such arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our

collaborators have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party in the territories included in the licenses. ~~54~~ We face significant competition in seeking appropriate collaborators. Whether we reach additional definitive agreements for collaborations will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration **,** and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of nonclinical and clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the U. S., the potential markets for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. The terms of any collaboration or other arrangements that we may establish may not be favorable to us. We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we ~~may~~ **will** need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. In addition, any future collaboration that we enter into may not be successful. The success of our **current and future** collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision- making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation. ~~We~~ **Our future growth** may ~~not~~ **depend, in part, on our ability to penetrate foreign markets, where we would** be **subject** ~~successful in our efforts~~ to ~~identify or discover~~ additional ~~CNS product candidates, or we~~ **regulatory burdens and other risks and uncertainties. Our future profitability** may ~~expend~~ **depend , in part,** ~~our limited resources to pursue a particular product candidate or indication and fail to capitalize~~ on ~~product candidates or indications that may be more profitable or for which there is a greater likelihood of success. The success of our business depends primarily upon~~ our ability to ~~identify,~~ develop and commercialize ~~CNS~~ **our** product candidates with ~~therapeutic~~ **third- party collaborators in foreign markets. If we develop** and **commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including: • our customers' ability to obtain reimbursement for our product candidates in foreign markets; • our inability to directly control** commercial **activities because we are relying on third parties; • the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements; • different medical practices and customs in foreign countries affecting acceptance in the marketplace; • import or export licensing requirements; • longer accounts receivable collection times; • longer lead times for shipping; • language barriers for technical training; • reduced protection of intellectual property rights, different standards of patentability and different availability of prior art in some foreign countries as compared with the U. S.; • the existence of additional** ~~potential~~ **potentially relevant third- party intellectual property rights; • foreign currency exchange rate fluctuations; and • the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute** . ~~We may~~ **Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. If we** fail to ~~pursue additional development opportunities~~ **comply with environmental, health and safety laws and regulations, we could become subject to fines** ~~for~~ **or penalties** ~~our~~ **or incur costs** ~~current CNS product candidates or identify additional CNS product candidates for development and commercialization for a number of reasons. Our research methodology may be unsuccessful in identifying new product candidates or our product candidates may be shown to have harmful side effects or may have other characteristics~~ that ~~may make the products unmarketable or unlikely to receive marketing approval. We strategically focus on a limited number of research and development programs and product candidates and are currently focused primarily on development of fasedienol and itruvone. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other potential CNS- related indications for fasedienol and / or itruvone that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it would~~ **could** ~~have been more advantageous for us to retain sole development and~~

~~commercialization rights to such product candidate. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would~~ have a material adverse effect on **the success of** our business ~~and could potentially cause us to cease operations~~ . ~~Research and development programs to identify and advance new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. 55~~ We are subject to **numerous environmental,** ~~healthcare~~ ---- **health and safety** laws and regulations **, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions** , which could ~~expose~~ **have a material adverse effect on our operations. Risks Related to Managing Our Business and Operations We depend heavily on our executive officers, third- party consultants and others and our ability to compete in the biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. The loss of their services or our inability to hire and retain such personnel would materially harm our business. Our success depends, and will likely continue to depend, upon our ability to hire, and our ability to retain the services of our executive officers and other key employees within our organization. Our executive officers and other key employees may terminate their employment with** us **at any time. The loss of their services might impede the achievement of our operational and strategic objectives. Our ability** to **compete in the biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific, medical, and technical personnel. In particular, we will need to retain and, in some cases, hire, qualified personnel with expertise in clinical development and operations, preclinical research and development, manufacturing, quality management, medical and regulatory affairs, finance and accounting and other areas in connection with the continued development and commercialization of our product candidates. We currently rely, and for the foreseeable future will continue to rely, on third- party consultants and advisors, including scientific and clinical advisors, to assist us in formulating certain of our research and development objectives and activities as well as the development of certain of our commercialization strategies. Our industry has experienced a high rate of turnover of management personnel in recent years. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully and the culture fit to be a leader in our organization. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Further, inflationary pressure may increase our costs, including employee compensation costs or result in employee attrition to the extent our compensation does not keep up with inflation, particularly if our competitors' compensation does. There can be no assurance that the services of third- party consultants and advisors will continue to be available to us on a timely basis when needed, that we will be able to manage our existing consultants and advisors or that we can find qualified replacements on economically reasonable terms, or at all. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified consultants and advisors, our ability to develop and commercialize our product candidates will be limited. We may not be able to hire and / or retain a sufficient number of employees or employees with the required expertise to develop our product candidates or operate our business successfully. As of March 31, 2024, we had 38 full- time employees. Our focus on the development of our lead product candidates requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot assure you that we will be able to hire and / or retain adequate staffing levels to develop our product candidates or run our operations and / or to accomplish all of the objectives that we otherwise would seek to accomplish. If we are not able to effectively expand our organization by hiring new qualified employees, our clinical trials may be delayed or terminated, we may not be able to successfully execute the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our development and commercialization goals. Our employees, independent contractors, consultants, collaborators and CROs may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation. We are exposed to the risk that our employees, independent contractors, consultants, collaborators and CROs may engage in fraudulent conduct or other illegal activity. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks**

or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Misconduct by those parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities that violates: • study and trial protocols or the FDA regulations or similar regulations of comparable non- U. S. regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; • manufacturing standards; • federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non- U. S. regulatory authorities; and • laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, integrity oversight and reporting obligations, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations. We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We expect to experience significant growth in the number of our employees and the scope of our operations. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of their attention to managing these growth activities. Due to our limited financial resources, our limited operating history and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or any necessary relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or any necessary relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates. Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by global political conditions, as well as general conditions in the global economy and in the global financial and stock markets. Global financial and political crises cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the economic downturn triggered by the COVID- 19 pandemic, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third- party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plan we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expense as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. Remote working arrangements could significantly increase the Company' s digital and cybersecurity risks. Most of our employees are geographically dispersed from our headquarters facility in South San Francisco and now routinely work remotely. With the continuing shift to remote working, and the use of virtual board and executive management meetings, cybersecurity risks are exponentially greater, including increased risk of phishing and other cybersecurity attacks as well as increased risk of

unauthorized dissemination of sensitive personal information or proprietary or confidential information about us or our customers, employees, or business partners. Despite our cybersecurity measures, we may be more susceptible to security breaches and other security incidents because we have less capability to implement, monitor, and enforce our information security and data protection policies. Techniques or software used to gain unauthorized access, and / or disable, degrade, or harm our systems may be difficult to detect for prolonged periods of time, and we may be unable to anticipate these techniques or put in place protective or preventive measures. The damage or disruption of our systems, or the theft or compromise of our technology, data, or intellectual property, may negatively impact our business, financial condition and results of operations, reputation, stock price and long- term value, which could adversely affect our business. Current politics in the U. S. could diminish the value of the pharmaceutical industry, thereby diminishing the value of our securities. The current political environment in the U. S. has led many incumbents and political candidates to propose various measures to reduce the prices for pharmaceuticals. These proposals may receive increasing publicity which, in turn, may cause the investing public to reduce the perceived value of pharmaceutical companies. Any decrease in the overall perception of the pharmaceutical industry may have an adverse impact on our share price and may limit our ability to raise capital needed to continue our drug development programs. Risks Related to Our Dependence on Third Parties We rely on third parties to assist in conducting our clinical trials. If they do not perform satisfactorily, we may not be able to obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed. We have relied upon and plan to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials and expect to rely on these third parties to conduct clinical trials of any product candidate that we develop. Our ability to complete clinical trials in a timely fashion depends on a number of key factors. These factors include protocol design, regulatory and IRB or ethics committee approval, patient enrollment rates and compliance with GCPs. We have opened clinical trial sites and are enrolling patients in a number of countries where our experience is limited. In most cases, we use the services of third parties, including CROs, to carry out our clinical trial- related activities and rely on such parties to accurately report their results. Our reliance on third parties for clinical development activities may impact or limit our control over the timing, conduct, expense and quality of our clinical trials. Moreover, the FDA and certain foreign regulatory authorities require us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA and comparable foreign regulatory authorities enforce these GCPs through periodic inspections of clinical trial sponsors, principal investigators, clinical trial sites and IRBs. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the U. S. Similar requirements may exist in foreign jurisdictions. We remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. Our failure or the failure of third parties to comply with the applicable protocol, legal and regulatory requirements and scientific standards can result in rejection of our clinical trial data or other sanctions. If we or our third- party clinical trial providers or third- party CROs do not successfully carry out these clinical activities, our clinical trials or the potential regulatory approval of a product candidate may be delayed or be unsuccessful. Additionally, if we or our third- party contractors fail to comply with applicable 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 product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA or comparable foreign regulatory authorities will determine that any of our clinical trials comply with GCPs. We are also required to register certain clinical trials and post the results of completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions **. Furthermore** , ~~civil~~ **the third** ~~penalties -- parties conducting clinical trials on our behalf are not our employees , contractual damages, reputational harm~~ and ~~diminished profits and future earnings. Although~~ **except for remedies available to us under our agreements with such independent contractors,** we **cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. Moreover, many CROs, including some of those that we have engaged to conduct our clinical trials, are experiencing enrollment challenges as a result of, among other things, high employee turnover driven by the post- COVID macroeconomic environment and the inexperience of new employees. Furthermore, at clinical trial sites, the availability of staff and trial participants has been limited due to a decrease in the number of clinical investigative sites across the globe. Accordingly, enrollment in some of our clinical trials may be slower than expected as a result of these changes in the post- COVID clinical trial landscape. These contractors 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 impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators,** do not **successfully carry out** ~~currently have any products on the~~ **their** ~~market~~ **contractual duties , meet expected deadlines** ~~once we begin commercializing our -- or conduct our clinical trials in accordance with CNS product candidates, we may be subject to additional healthcare statutory and~~ regulatory requirements **or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such** ~~and -~~ **an** ~~enforcement~~ **event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our**

costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed. We also rely on other third parties to manufacture, store and distribute drug supplies for our clinical trials. Any performance failure on the part of these third- parties could delay clinical development or regulatory approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue. Any of the third- party organizations we utilize may terminate their engagements with us under certain circumstances. The replacement of an existing CRO or other third party may result in the delay of the affected trials or otherwise adversely affect our efforts to obtain regulatory approvals and commercialize our product candidates. Although we believe we have diversified our risk by **engaging a number of CROs and** ~~the~~ **other** ~~federal government~~ **third- party organizations** and ~~the~~ **there** ~~states and foreign governments~~ **are a number of other CROs we could engage to continue these activities, we may not be able to enter into alternative arrangements or do so on commercially reasonable terms or** in **a timely manner. In addition, while we believe there may be suitable replacements for one or more of these service providers, there is a natural transition period when a new service provider begins work. As a result, delays may occur,** which ~~we conduct~~ **could negatively impact our ability to meet our expected clinical development timelines and harm** our business **, financial condition and prospects** . ~~Healthcare~~ **In particular, we plan to rely on a hybrid functional service provider (FSP), approach, where, rather than relying on a small number of third- party services** providers **for a full suite of services** , ~~physicians~~ **we plan to use a wider number of third- party service providers on** ~~and~~ **an** ~~others~~ **à la carte basis grouped by specific function. We may not be able to realize the cost savings typically associated with the hybrid FSP approach, or this approach may require us to incur increased startup or integration costs. Our hybrid FSP approach may also require us to manage and monitor an increased number of service providers and contractual relationships. Finally, this approach may require us to handle certain functions internally rather than outsourcing them to third parties. Handling these functions internally may require us to spend more time and capital hiring and training employees, and any failure to do so successfully may negatively impact our operations. Our use of third parties to manufacture our product candidates may increase the risk that we** will ~~play~~ **not have sufficient quantities of our product candidates, raw materials, active pharmaceutical ingredients (APIs) or drug products when needed or at an acceptable cost. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. Our current strategy is to outsource all manufacturing of our product candidates to third parties. We currently rely on and engage third- party manufacturers to provide all of the API and the final drug product formulation of all of our product candidates that are being used in our clinical trials and preclinical studies. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement. However, if necessary, we can provide no assurance that we will be able to find an alternative manufacturer on acceptable terms. We may not be able to timely secure needed supply arrangements on satisfactory terms, or at all. Our failure to secure these arrangements as needed could have** a ~~primary role in~~ **material adverse effect on our ability to complete** the **development** ~~recommendation and prescription~~ of our product candidates **or, to commercialize them** , if approved. ~~Our future~~ **We may be unable to conclude agreements for commercial supply with third- party manufacturers or may be unable to do so on acceptable terms. There may be difficulties in scaling up to commercial quantities and formulation of our product candidates, and the costs of manufacturing could be prohibitive. Many of the third- party manufacturers we rely on have only recently begun working with us and have limited or no experience manufacturing our API and final drug products. If our manufacturers have difficulty or suffer delays in successfully manufacturing material that meets our specifications, it may limit supply of our product candidates and could delay our clinical trials. Even if we are able to establish and maintain** arrangements with third- party ~~payers~~ **manufacturers, reliance on third- party manufacturers entails additional risks, including: • the failure of the third- party manufacturer to comply with applicable regulatory requirements and reliance on third parties for manufacturing process development, regulatory compliance and quality assurance; • manufacturing delays if our third- party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us; • limitations on supply availability resulting from capacity and scheduling constraints of third parties; • the possible breach of manufacturing agreements by third parties because of factors beyond our control; • the possible termination or non- renewal of the manufacturing agreements by the third party, at a time that is costly or inconvenient to us; and • the possible misappropriation of our proprietary information, including our trade secrets and know- how. If we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability to obtain regulatory approval for our product candidates. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other foreign regulatory authorities. Additionally, if any third- party manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different manufacturer. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back- up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change third- party manufacturers for any reason, we** will **be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new**

manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. We may be unsuccessful in demonstrating the comparability of clinical supplies, which could require the conduct of additional clinical trials. The delays associated with the verification of a new third-party manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third- party manufacturer may possess technology related to the manufacture of our product candidate that such third party owns independently. This would increase our reliance on such third- party manufacturer or require us to obtain a license from such third- party manufacturer in order to have another third party manufacture our product candidates. If any of our product candidates is approved by any regulatory agency, we intend to utilize arrangements with third- party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization. Some of our manufacturers are located outside of the U. S. There is currently significant uncertainty about the future relationship between the U. S. and various other countries, including China, with respect to trade policies, treaties, government regulations and tariffs. Increased tariffs could potentially disrupt our existing supply chains and impose additional costs on our business. Additionally, it is possible further tariffs may be imposed that could affect imports of APIs used in our product candidates, or our business may be adversely impacted by retaliatory trade measures taken by China or other countries, including restricted access to such raw materials used in our product candidates. Given the unpredictable regulatory environment in China and the U. S. and uncertainty regarding how the U. S. or foreign governments will act with respect to tariffs, international trade agreements and policies, further governmental action related to tariffs, additional taxes, regulatory changes or other retaliatory trade measures in the future could occur with a corresponding detrimental impact on our business and financial condition. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or voluntary recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. The facilities used by our contract manufacturers to manufacture our product candidates must be evaluated by the FDA or comparable foreign regulatory authorities in connection with any NDA or other application we may submit. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs and similar foreign requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we may not be able to secure and / or maintain regulatory approval for our product candidates manufactured at these facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA finds deficiencies or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP and similar foreign requirements or other FDA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products, if approved. The FDA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with cGMPs and similar foreign requirements. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP or similar foreign requirements. Any failure to comply with cGMP requirements or other FDA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval, if obtained. Failure of any third- party manufacturer to comply with cGMP requirements for applicable drug / device combination products could significantly affect supplies of our product candidates. We expect our pherine product candidates, fasedienol, ituruvone, PH15, PH80 and PH284, will be considered drug- device combination products. Third- party manufacturers may not be able to comply with cGMP requirements applicable to drug / device combination products, including applicable provisions of the FDA' s or a comparable foreign regulatory authority' s drug cGMP regulations, device cGMP requirements embodied in the Quality System Regulation (QSR) or similar regulatory requirements outside the U. S. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in material adverse effects, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. If any third- party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates or increase the product yield of its manufacturing, then our manufacturing costs may increase and commercialization may be delayed. In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates, our third- party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of our

product candidates. The transition to larger scale production could prove difficult. In addition, if our third- party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the same quality then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operations. We may need to maintain licenses for APIs from third parties to develop and commercialize some of our product candidates, which could increase our development costs and delay our ability to commercialize those product candidates. Should we decide to use any APIs in any of our product candidates that are proprietary to one or more third parties, we would need to maintain licenses to those APIs from those third parties. If we are unable to gain or continue to access rights to these APIs prior to conducting preclinical toxicology studies intended to support clinical trials, we may need to develop alternate product candidates from these programs by either accessing or developing alternate APIs, resulting in increased development costs and delays in commercialization of these product candidates. If we are unable to gain or maintain continued access rights to the desired APIs on commercially reasonable terms or develop suitable alternate APIs, we may not be able to commercialize product candidates from these programs. Risks Related to Government Regulation Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable foreign regulatory authorities must also approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the U. S., including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U. S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the U. S. have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. 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 products in certain countries. If we fail to comply with the regulatory requirements in international markets and / or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed. Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates. If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing studies and submission of safety, efficacy and other post- market information, including both federal and state requirements in the U. S. and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and similar foreign requirements and GCP requirements for any clinical trials that we conduct post- approval. Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP and similar foreign regulations and applicable product tracking and tracing requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and similar foreign requirements and adherence to commitments made in any NDA, other marketing application and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. Certain endpoint data we hope to include in any approved product labeling also may not make it into such labeling, including exploratory or secondary endpoint data such as patient- reported outcome measures. The FDA may also require a REMS, program as a condition of approval of our product candidates, which could entail requirements for long- term patient follow- up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post- marketing information and reports and registration. The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post- market studies or clinical trials to assess new safety risks or imposition of distribution restrictions or

other restrictions under a REMS program. Other potential consequences include, among other things: • restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary product recalls; • fines, warning letters or holds on clinical trials; • refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of approvals; • product seizure or detention or refusal to permit the import or export of our product candidates; and • injunctions or the imposition of civil or criminal penalties. Additionally, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product' s ability to be marketed. The FDA and certain foreign regulatory authorities strictly regulate marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The policies of the FDA and comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U. S. 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. While we may in the future seek designations for our product candidates with the FDA and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process, an accelerated regulatory pathway or regulatory exclusivity, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations. The FDA and comparable foreign regulatory authorities offer certain designations for product candidates. These programs are designed to encourage the research and development of product candidates that are intended to address serious conditions. These designations may confer benefits such as additional interaction with regulatory authorities and eligibility for expedited review procedures. However, there can be no assurance that we will successfully obtain such designations for our product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for our product candidates, there can be no assurance that we will realize their intended benefits. For example, we may seek a Breakthrough Therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For a product candidate that have been designated as a Breakthrough Therapy, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates receiving Breakthrough Therapy designation also receive the same benefits associated with Fast Track designation, described below. Designation as a Breakthrough Therapy is within the sole discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification. Furthermore, the FDA has granted Fast Track designation for fasedienol for the acute treatment of SAD, for itruvone for the treatment of MDD, and for AV- 101 for the adjunctive treatment of MDD and for the treatment of NP, and we may seek Fast Track Designation for some of our other product candidates. If a drug or biologic is intended for the treatment of a serious or life- threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may be eligible for Fast Track designation. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. An NDA submitted for a Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. The receipt of Fast Track designation for fasedienol for acute treatment of SAD, for itruvone for the treatment of MDD and AV- 101 for the adjunctive treatment of MDD and for the treatment of neuropathic pain, and any future receipt of Fast Track designation for other product candidates, does not guarantee a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Some of our programs may be partially supported

by government grant awards, which may not be available to us in the future or subject us to federal regulations such as " march- in " rights, certain reporting requirements and a preference for U. S. industry. To fund a portion of our future research and development programs, we may apply for grant funding from governmental agencies. However, funding by these governmental agencies may be significantly reduced or eliminated in the future for a number of reasons. For example, some programs are subject to a yearly appropriations process in Congress. In addition, we may not receive full funding under current or future grants because of budgeting constraints of the agency administering the program or unsatisfactory progress on the study being funded. Therefore, we cannot assure you that we will receive any future grant funding from any government agencies, or, that if received, we will receive the full amount of the particular grant award. Any such reductions could delay the development of our product candidates. Moreover, any intellectual property rights generated through the use of U. S. government funding are subject to the Bayh- Dole Act of 1980 (Bayh- Dole Act). These U. S. government rights in certain inventions developed under a government- funded program include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right to require us to grant exclusive, partially exclusive, or non- exclusive licenses to any of these inventions to a third party if the government determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations, which we refer to as march- in rights. The U. S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government, elect title, and file an application to register the intellectual property within specified time limits. In addition, the U. S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government- funded program is also subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U. S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U. S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U. S. or that under the circumstances domestic manufacture is not commercially feasible. As a result of any arrangement involving government funding, and if we make inventions as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh- Dole Act. To the extent any of our current or future intellectual property is generated through the use of U. S. government funding, the provisions of the Bayh- Dole Act may similarly apply. Any exercise by the government of certain of its rights could harm our competitive position, business, financial condition, results of operations and prospects. Our relationships with healthcare providers and physicians and third- party payors will be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us **to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. Healthcare providers, physicians and third- party payors in the U. S. and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third- party payors and customers can expose pharmaceutical manufacturers** to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we **conduct research and would sell,** market ~~, sell~~ and distribute our ~~product~~ **products** ~~candidates, if we obtain marketing approval~~ . ~~Restrictions under applicable federal~~ **Federal** and state healthcare laws and regulations **that may affect our ability to operate** include the following: ~~● The~~ **• the** federal ~~anti~~ **Anti** - ~~kickback~~ **Kickback** ~~statute~~ **Statute , which** prohibits, among other things, persons **or entities** from knowingly and willfully soliciting, **receiving,** offering ~~, receiving~~ or ~~providing~~ **paying any** remuneration **(including any kickback, bribe or rebate)** , directly or indirectly, **overtly or covertly,** in cash or in kind, to induce **,** or **in return** ~~reward either the referral of an individual~~ for ~~, or~~ the purchase, **lease,** order **, arrangement,** or recommendation of ~~,~~ any good **, facility, item** or service ~~,~~ for which payment may be made **, in whole or in part,** under **a** federal healthcare ~~programs~~ - **program,** such as **the** Medicare and Medicaid **programs** . ~~● The~~ **A person or entity does not need to have actual knowledge of the federal Anti- Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil fines and criminal penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the** federal False Claims Act **or federal civil money penalties; • the federal civil and criminal false claims laws and civil monetary penalty laws, such as the federal False Claims Act, which** ~~imposes~~ **impose** criminal and civil penalties **and authorize** ~~, including those from~~ civil whistleblower or qui tam actions, against individuals or entities for **, among other things:** knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent ~~or~~ **; knowingly** making **, using or causing to be made or used,** a false statement **of record material** to **a false** ~~avoid, decrease,~~ or **fraudulent claim or obligation to pay or transmit money or property to the federal government or knowingly** ~~conceal~~ **concealing or knowingly and improperly avoiding or decreasing** an obligation to pay money to the federal government. ~~●~~ **Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to " cause " the submission of false or fraudulent claims.** The **federal False Claims Act also permits a private individual acting as a " whistleblower " to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery; • the** federal Health Insurance Portability and Accountability Act of 1996 **(HIPAA)** , ~~as amended by~~ **which prohibits, among** ~~the~~ **other things** ~~Health Information Technology for Economic and Clinical Health Act~~ , ~~imposes criminal~~ **a person from knowingly** and **willfully** ~~civil liability for~~

executing , or attempting to execute, a scheme to defraud any healthcare benefit program or obtain ~~and also imposes obligations~~ , by means ~~including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission~~ of ~~individually identifiable health information. ● The federal~~ false ~~statements statute prohibits~~ or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e. g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false , fictitious, or fraudulent ~~statement~~ statements or representations in connection with the delivery of , or payment for , healthcare benefits, items or services relating to healthcare matters . ~~● The~~ Similar to the federal ~~transparency requirements~~ Anti- Kickback Statute , ~~sometimes referred~~ a person or entity does not need to ~~as~~ have actual knowledge of the ~~"~~ statute or specific intent to violate it in order to have committed a violation; • the federal Physician Payments Sunshine Act, which ~~" under the Patient Protection and Affordable Care Act, require~~ requires applicable manufacturers of drugs, devices, biologics and medical supplies ~~that are reimbursable~~ for which payment is available under Medicare, Medicaid ~~,~~ or the Children' s Health Insurance Program to report annually to the U. S. Centers for Medicare & Medicaid Services, within the U. S. Department of Health and Human Services , information related to ~~physician~~ payments ~~and~~ or other transfers of value ~~and~~ made to physicians, certain non- physician practitioners including nurse practitioners, certified nurse anesthetists, anesthesiologist assistants, physician assistants, clinical nurse specialists, and certified nurse midwives as well as teaching hospitals and to disclose ownership and investment interests held by physicians and their immediate family members; • federal government price reporting laws, which require manufacturers to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers . ~~● Analogous~~ Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above , ~~such as~~ among others, some of which may be broader in scope and may apply regardless of the payor. Many U. S. ~~state~~ states have adopted laws similar to the federal ~~anti~~ Anti - ~~kickback~~ Kickback Statute and ~~false~~ False ~~claims~~ Claims Act ~~laws and transparency laws~~ , and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental ~~third- party payers~~ payors , including private insurers . In addition , ~~and~~ some ~~state~~ states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for ~~pharmaceutical~~ Pharmaceutical ~~industry~~ Manufacturers and / or the Pharmaceutical Research and Manufacturers of America ' s Code on Interactions with Healthcare Professionals ~~voluntary compliance guidelines and the relevant compliance~~ . Several states also impose ~~● Guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and~~ other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers , which has led ~~or marketing expenditures and drug pricing. ● Foreign Corrupt Practices Act and its application~~ to ~~marketing~~ a number of investigations, prosecutions, convictions and ~~selling practices~~ settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to ~~clinical trials~~ possible investigations by government authorities, can be time and resource- consuming and can divert a company' s attention from the business . ~~56~~ Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations ~~could be costly~~ will involve substantial costs . It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations , agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations ~~were~~ are found to be in violation of any of ~~these~~ -- the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including administrative, civil ~~,~~ and criminal ~~and administrative~~ penalties, damages, fines ~~and~~ , disgorgement, the exclusion from ~~government funded~~ participation in federal and state healthcare programs, individual imprisonment, reputational harm and the curtailment or restructuring of our operations, as well as 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. Further, defending against any such ~~as Medicare~~ actions can be costly and ~~Medicaid~~ time consuming , and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any ~~of which could substantially disrupt~~ such actions that may be brought against us, our ~~operations~~ business may be impaired . If any of the physicians or other providers or entities with whom we expect to do business ~~are~~ is found to not be in ~~out of~~ compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government - funded healthcare programs ~~. The FDA~~ and imprisonment ~~other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses~~ . If any ~~we are found to have improperly promoted off- label uses~~ of ~~-~~ the above occur , our ~~we may become subject to significant liability~~ -- ability ~~. The FDA~~ to operate our business and our results of operations could ~~other regulatory agencies strictly regulate the promotional claims that may~~ be ~~made about prescription~~ adversely affected. Coverage and reimbursement may be limited or unavailable in certain market segments for our ~~products~~ - product candidates , if approved ~~. In particular~~ , which could make it difficult ~~a product may not be promoted~~ for us to sell ~~uses that are not approved by the FDA or such other regulatory agencies as reflected in the product' s approved labeling. For example, if we receive FDA marketing approval for fasedienol as an~~ any product candidates profitably ~~needed treatment of anxiety in adults with SAD, physicians may prescribe fasedienol to their patients in a manner that is inconsistent with the FDA- approved label. However, if~~

~~we are found to have promoted such off- label uses, we may become subject to significant liability~~ . The **success** ~~federal government has levied large civil and criminal fines against companies for alleged improper off- label promotion and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion~~ of our product candidates, if approved, **depends on the** ~~we could become subject to significant liability~~ - **availability of coverage** ~~, which would materially adversely affect our business~~ and **adequate** ~~financial condition. Even if approved,~~ reimbursement **from** ~~policies could limit our ability to sell our CNS product candidates. Market acceptance and sales of our product candidates will depend heavily on reimbursement policies and may be affected by healthcare reform measures. Government authorities and~~ third- party ~~payers~~ **payors . We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. Patients who are provided medical treatment for their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Government authorities and other third- party payors** , such as private health insurers and health maintenance organizations, decide which ~~medications~~ **drugs and treatments** they will **cover** ~~pay for~~ and ~~establish~~ **the amount of** reimbursement ~~levels for those medications~~ . ~~Cost containment is~~ **Coverage and reimbursement by** a ~~primary concern in the United States healthcare industry and elsewhere. Government authorities and these~~ third- party ~~payers have attempted to control~~ **payor may depend upon a number of factors, including the third- party payor' s determination that use of a product is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; •** ~~costs~~ - **cost** ~~by limiting~~ **- effective; and • neither experimental nor investigational. In the U. S., no uniform policy of** coverage and ~~the amount of~~ reimbursement for ~~particular medications~~ **products exists among third- party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third- party payor is a time- consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost- effectiveness data for the use of our products on a payor- by- payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Private health insurers and other third- party payors in the U. S. often follow the coverage and reimbursement policies of government payors, including the Medicare or Medicaid programs. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co- payments that patients find unacceptably high. Additionally, third- party payors may not cover, or provide adequate reimbursement for, long- term follow- up evaluations required following the use of product candidates, once approved. Patients are unlikely to use our product candidates, once approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of their cost. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third- party payors will decide with respect to the coverage and reimbursement for our product candidates. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U. S. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products** . We cannot be sure that reimbursement will be available for ~~our~~ **any** product ~~candidates~~ - **candidate that we commercialize** and, if reimbursement is available, the level of ~~such~~ reimbursement ~~. Reimbursement may impact the demand for, or the price of, our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates. In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidates with other available therapies. If reimbursement for our product candidates is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected. We may seek FDA Orphan Drug designation for one or more of our CNS product candidates. Even if we have obtained FDA Orphan Drug designation for a product candidate, there may be limits to the regulatory exclusivity afforded by such designation. We may, in the future, choose to seek FDA Orphan Drug designation for one or more of our current or future CNS product candidates. Even if we obtain Orphan Drug designation from the FDA for a product candidate, there are limitations to the exclusivity afforded by such designation. In the U. S., the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA to market the same drug for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. 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. To obtain Orphan Drug status for a drug that shares the same active moiety as an already approved drug, it must be demonstrated to the FDA that the drug is safer or more effective than the approved orphan designated drug, or that it makes a major contribution to patient care~~ . In addition, ~~a designated orphan drug may~~ **many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are** not ~~receive orphan drug exclusivity if it is approved~~ **submitted**

accurately and timely. Further, these prices for ~~a use that is broader than the indication for which it received orphan designation. In addition, orphan drug~~ **drugs** ~~exclusive marketing rights in the U. S.~~ may be **reduced by mandatory discounts** ~~lost if the FDA later determines that the request for~~ **or rebates required by government healthcare programs** ~~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 or if another drug with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care~~ . **Payment methodologies** ~~57 Our future growth~~ may ~~depend, in part, on our ability to penetrate foreign markets, where we would~~ be subject to ~~additional~~ **changes in healthcare legislation and** regulatory ~~burdens~~ **initiatives. Moreover, increasing efforts by governmental** and other ~~risks and uncertainties. Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties such as our collaboration with AffaMed to develop and commercialize fasedienol in key Asian markets. If we commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including: ● our customers' ability to obtain reimbursement for our product candidates in foreign markets; ● our inability to directly control commercial activities because we are relying on third parties; ● the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements; ● different medical practices and customs in foreign countries affecting acceptance in the marketplace; ● import or export licensing requirements; ● longer accounts receivable collection times; ● longer lead times for shipping; ● language barriers for technical training; ● reduced protection of intellectual property rights, different standards of patentability and different availability of prior art in some foreign countries as compared with the U. S.; ● the existence of additional potentially relevant~~ third- party **payors** ~~intellectual property rights; ● foreign currency exchange rate fluctuations; and ● the interpretation of contractual provisions governed by foreign laws~~ in the ~~event~~ **U. S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level** of **reimbursement for newly approved products and, as** a ~~contract dispute. Foreign sales of~~ **result, they may not cover or provide adequate payment for** our product candidates ~~could also be adversely affected by~~ **. There has been increasing legislative and enforcement interest in the U. S. with respect to specialty drug pricing practices. Specifically,** ~~the~~ **there** ~~imposition~~ **have been several recent U. S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost** of **prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform** ~~governmental~~ **government program reimbursement methodologies for drugs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to** ~~controls~~ **control pharmaceutical** ~~, political~~ and ~~economic instability~~ **biological product pricing** , ~~trade~~ **including price or patient reimbursement constraints, discounts,** restrictions **on certain product access** and **marketing** ~~changes in tariffs. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs~~ **cost** ~~that could~~ **disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Ongoing healthcare legislative and regulatory reform measures may** have a material adverse effect on ~~the success of~~ our business **and results of operations. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example, (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products or (iv) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical products, limiting coverage and the amount of reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the U. S. Governments have shown significant interest in implementing cost- containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. For instance, in August 2022, the Inflation Reduction Act of 2022 (the IRA) was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that allow the U. S. government to negotiate Medicare Part B and Part D pricing for certain high- cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, create an out- of- pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D and delay the rebate rule that would require pass- through of pharmacy benefit manager rebates to beneficiaries. In particular, the IRA allows CMS to begin negotiating prices for certain high- cost Medicare- covered small molecule drugs after they have spent seven years on the market. On August 29, 2023, CMS announced the list of the first ten drugs that will be subject to price negotiations. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. All of our disclosed product candidates are small molecule drugs and certain of them are being developed in indications that may rely heavily on Medicare reimbursement, such as depression. Accordingly, these new price- negotiation provisions may have a negative impact on our future revenue and profits. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA' s Medicare drug price negotiation program. The effect of IRA on our business and the healthcare industry in general is not yet fully known. Adoption of price controls and cost- containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our revenue generated from the sale of any approved products. Even if we do receive a favorable coverage determination for our products by third- party payors, coverage policies and third- party payor reimbursement rates may change at any time. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been**

heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal 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 pharmaceutical products. Congress has indicated that it will continue to seek new legislative measures to control drug costs. The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect: • the demand for any of our product candidates, if approved; • the ability to set a price that we believe is fair for any of our product candidates, if approved; • our ability to generate revenues and achieve or maintain profitability; • the level of taxes that we are required to pay; and • the availability of capital . We **expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals or clearances of our product candidates, if any, may be. Off- label use or misuse of our product candidates may harm our reputation in the marketplace or result in injuries that lead to costly product liability suits. If our product candidates** are **approved by the FDA or comparable foreign** ~~subject to numerous environmental, health and safety laws and regulations~~ **regulatory authorities, we may only promote or market our product candidates in a manner consistent with their FDA- approved labeling (or the label approved by foreign regulatory authorities). We will train our marketing and sales force against promoting our product candidates for uses outside of the approved indications for use, known as " off- label uses. " We cannot, however, prevent a physician from using our product candidates off- label, when in the physician' s independent professional medical judgment he or she deems it appropriate. Furthermore, the use of our product candidates for indications other than those approved by the FDA or comparable foreign regulatory authorities may not effectively treat such conditions. Any such off- label use of our product candidates could harm our reputation in the marketplace among physicians and patients. There may also be increased risk of injury to patients if physicians attempt to use our product candidates for these uses for which they are not approved, which could lead to product liability suits that might require significant financial and management resources and that could harm our reputation. Inadequate funding for the FDA or other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA and comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the FDA and comparable foreign regulatory authorities, have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely** , including those ~~governing laboratory procedures~~ **that fund research** and **development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA,** ~~the~~ **other government agencies** ~~handling, use, storage, treatment~~ and **comparable foreign regulatory authorities may also slow** ~~disposal of hazardous materials and wastes. Our operations involve~~ the ~~use of hazardous~~ **time necessary for new drugs to be reviewed** and ~~flammable materials~~ **/ or approved by necessary government agencies and comparable foreign regulatory authorities, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs** , including **as a** ~~chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting~~ --- **result** ~~from our use~~ of ~~hazardous materials~~ **reaching the debt ceiling** , ~~we it~~ could ~~be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant~~ **significantly impact** ~~costs associated with civil or criminal fines and penalties. 58 Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from~~ the ~~use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability~~ -- **ability of the FDA and comparable foreign regulatory authorities to timely review and process** ~~or~~ **our** ~~toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations~~ - **regulatory submissions** . ~~These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions~~ , which could have a material adverse effect on our **business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our** operations. **Separately** ~~Risks Related to Our Financial Position We have incurred significant net losses since inception~~ , ~~and we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability, which would depress the market price of our common stock and could cause you to lose all or a part of your investment. We have incurred significant net losses~~ in **response** ~~each fiscal year since our inception in 1998, including net losses of approximately $ 59. 2 million and $ 47. 8~~

million during our fiscal years ended March 31, 2023 and 2022, respectively. At March 31, 2023, we had an accumulated deficit of approximately $ 326. 9 million and our auditors have included a qualification to their opinion on our Financial Statements at March 31, 2023 as a result of the uncertainty of our ability to continue as a going concern. We do not know whether or when we will become profitable. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expense to significantly increase in connection with planned nonclinical and clinical studies, and out- sourced manufacturing, of our product candidates. As a public company, we incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. Our ability to become profitable depends upon our ability to generate recurring revenues. Through March 31, 2023, we have generated approximately $ 22. 7 million in revenues, consisting of receipts of non- dilutive cash payments from collaborators, sublicense revenue, including the $ 5. 0 million cash payment received under the AffaMed Agreement during the quarter ended September 30, 2020, the majority of which remains recorded as deferred revenue at March 31, 2023, and research and development grant awards from the NIH. We have not yet commercialized any product or generated any revenues from product sales, and we do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to experience sales of our current and / or future CNS product candidate, or we enter into one or more development and commercialization agreements with respect our current CNS product candidates or one or more other future CNS product candidates. Our ability to generate recurring revenue depends on a number of factors, including, but not limited to, our ability to: ● initiate and successfully complete nonclinical and clinical trials that meet their prescribed endpoints; ● initiate and successfully complete all safety studies required to obtain U. S. and foreign marketing approval for our CNS product candidates; ● timely complete and compose successful regulatory submissions such as NDAs or comparable documents for both the U. S. and foreign jurisdictions; ● commercialize our CNS product candidates, if approved, by developing a sales force and / or entering into collaborations with third parties for sales and marketing capabilities; and ● achieve market acceptance of our CNS product candidates in the medical community and with third- party payers. 59 Current volatile and / or recessionary economic conditions in the U. S. or abroad could adversely affect our business or our access to capital markets in a material manner. To date, our principal sources of capital used to fund our development programs and other operations have been the net proceeds we received from sales of equity securities. We have and will continue to use significant capital for the development of our product candidates, and, as such, we expect to seek additional capital from future issuance (s) of our securities, which may consist of issuances of equity and / or debt securities, to fund our planned operations. Accordingly, our results of operations and the implementation of both our short- term and long- term business plan could be adversely affected by general conditions in the global economy, including conditions that are outside of our control. A prolonged economic downturn could result in a variety of risks to our business and may have a material adverse effect on us, including limiting or restricting our ability to access capital on favorable terms, or at all, which would limit our ability to obtain adequate financing to maintain our operations. We previously identified material weaknesses in our internal control over financial reporting, and we may identify future material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we fail to establish and maintain adequate internal control over financial reporting, we may not be able to produce timely and accurate financial statements, and we may conclude that our internal control over financial reporting is not effective, which may adversely affect our business. We previously identified material weaknesses in our internal control over financial reporting that, as of March 31, 2022, were remediated. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim condensed consolidated financial statements will not be prevented or detected on a timely basis. Although we have determined that the previously identified material weaknesses have been remediated as of March 31, 2022, we cannot assure you that we will not identify other material weaknesses in the future, which could negatively impact our results of operations in future periods. Ensuring that we have adequate internal control over financial reporting so that we can produce accurate financial statements on a timely basis is a costly and time- consuming effort that needs to be re- evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. Implementing any future changes to our internal control over financial reporting may entail substantial costs to hire additional personnel, modify our existing processes and will take significant time to fully implement. These changes may not, however, be effective in establishing and maintaining the adequacy of our internal control, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. Any failure to maintain or implement required effective internal control over financial reporting, or any difficulties we encounter in their implementation, could result in additional material weaknesses, cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. Furthermore, if we cannot provide reliable financial reports or prevent material misstatements due to fraud or error, our business and results of operations could be harmed, and investors could lose confidence in our reported financial information. We also could become subject to investigations by The Nasdaq Stock Market, the Securities and Exchange Commission or other regulatory authorities, which could require additional financial and management resources. 60 Raising additional capital is likely to cause substantial dilution to our existing stockholders, may restrict our operations or require us to relinquish rights, and may require us to seek stockholder

approval to authorize additional shares of our common stock. We may pursue private and public equity offerings, debt financings, and strategic acquisitions, collaborations and licensing arrangements in the future. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, or to the extent, for strategic purposes or in the context of strategic acquisitions, we issue shares of common stock, our current stockholders' ownership interest in our company will be substantially diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and would involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic acquisitions, partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us. We may be required to raise additional financing by issuing new securities with terms or rights superior to those of our existing securityholders, which could adversely affect the market price of shares of our common stock and our business. We will require substantial additional financing to fund future operations, including research and development activities for our CNS product candidates, assuming our clinical development programs are successful and we receive necessary regulatory approvals from the FDA. We may not be able to obtain financing on favorable terms, if at all. If we raise additional funds by issuing equity securities, the percentage ownership of our current stockholders will be reduced, and the holders of the new equity securities may have rights superior to those of our existing security holders, which could adversely affect the market price of our common stock and the voting power of shares of our common stock. If we raise additional funds by issuing debt securities, the holders of these debt securities would similarly have some rights senior to those of our existing securityholders, and the terms of these debt securities could impose restrictions on operations and create a significant interest expense for us, which could have a materially adverse effect on our business. Our ability to use net operating losses to offset future taxable income is subject to certain limitations. As of March 31, 2023, we had federal and state net operating loss carryforwards of approximately $ 191. 9 million and $ 65. 2 million, respectively, which have begun to expire in fiscal 2022 and will continue to expire in future periods. Under Section 382 of the Internal Revenue Code of 1986, as amended (the Code), changes in our ownership may limit the amount of our net operating loss carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50 % within a three- year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Any such limitation, whether as the result of prior or future offerings of our debt and / or equity securities, private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us could have a material adverse effect on our results of operations in future years. We have not yet completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study. General Company- Related Risks If we fail to retain and attract senior management and key scientific personnel, we may be unable to successfully produce and develop our product candidates. Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and technical personnel across multiple key functions, including, but not limited to clinical operations, finance, legal, human resources, information technology, CMC and quality assurance, regulatory affairs and medical affairs. We are highly dependent upon our Chief Executive Officer and Chief Financial Officer, as well as our other senior management personnel, advisors, consultants and scientific and clinical collaborators. As of the date of this Report, we have 33 full- time employees, which may make us more reliant on our individual employees than companies with a greater number of employees. The loss of services of any of these individuals could delay or prevent the successful development of our product candidates or disrupt our administrative functions. 61 Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems following our change in business plans as a result of the negative results of our PALISADE- 1 clinical trial or in the future. As of the date of this Report, a total of nine employees have voluntarily resigned from their positions within the Company since the PALISADE- 1 outcome was reported, including our Chief Commercial Officer and Chief Medical Officer. Work conducted by these individuals that furthers our current business plan has assumed by other employees and, when appropriate, based on clinical, regulatory and financial considerations, may be resumed by personnel hired in the future. However, competition for qualified personnel in the pharmaceuticals field is intense, and we may not be able to attract and retain quality personnel on acceptable terms. In addition, we rely on a broad and diverse range of strategic consultants and advisors, including manufacturing, nonclinical and clinical development and regulatory advisors and CMOs and CROs, to assist us in designing and implementing our research and development and regulatory strategies and plans for our product candidates. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. As we seek to advance development of our product candidates, we will need to further expand our research and development capabilities and our contractual arrangements with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to develop our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our research, development and regulatory efforts effectively, and hire, train and integrate additional management, administrative, research and development, regulatory and other personnel. The hiring, training and integration of new employees may be more difficult, costly and / or time- consuming for us because we have fewer resources than a larger organization. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing the Company. If product liability lawsuits are brought against us, we may incur substantial liabilities and

may be required to limit commercialization of our product candidates. As we develop our product candidates, either on our own or in collaboration with others, we will face inherent risks of product liability as a result of the required clinical testing of such product candidates and will face an even greater risk if we or our collaborators commercialize any such product candidates. For example, we may be sued if any of the product candidates we or our collaborators develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: ● decreased demand for product candidates that we may develop; ● injury to our reputation; ● withdrawal of clinical trial participants; ● costs to defend the related litigation; ● a diversion of management' s time and our resources; ● substantial monetary awards to trial participants or patients; or ● product recalls, withdrawals or labeling, marketing or promotional restrictions. 62 Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. Although we currently maintain general and product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by global political conditions, as well as general conditions in the global economy and in the global financial and stock markets. Global financial and political crises cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the economic downturn triggered by the COVID-19 pandemic, **the FDA postponed most inspections** could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at **domestic and** all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing --- **foreign manufacturing facilities** could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster **March 2020 until July 2021** . Natural disasters could severely disrupt our **Even though the FDA has since resumed standard inspection** operations, and have a material adverse effect on **any resurgence of the virus may lead to other inspectional** our **or administrative delays** business, results of operations, financial condition and prospects. If a natural disaster **prolonged government shutdown occurs** , power outage **or if global health concerns continue to hinder or prevent the FDA** or other **regulatory authorities** event occurred that prevented us from **conducting** using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third **their regular inspections** - party CMOs , **reviews,** or **other regulatory activities** that otherwise disrupted operations , it **could significantly impact the ability of the FDA** may be difficult or, in certain cases, impossible for **or** us **other regulatory authorities** to continue our business for a substantial period of time **timely review** . The disaster recovery and **process** business continuity plans we have in place may prove inadequate in the event of a serious disaster or **our regulatory submissions** similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans , which could have a material adverse effect on our business. Our business **We are subject to evolving global data protection laws** and **regulations, which may require us to incur substantial compliance costs** operations would suffer in the event of cybersecurity or other system failures. Our business depends on complex information systems , and any failure to successfully maintain these systems or implement new systems to handle our **or perceived failure by us to comply with such laws and regulations may** changing needs could result in a material disruption of our product candidates' development programs or otherwise materially harm our **business and** operations. **The global** In the ordinary course of our business, we collect and store sensitive data **protection landscape is rapidly evolving** , including intellectual property, **and we may be** our **or become subject to** proprietary business information and that of our **or** suppliers **affected by numerous federal, state and foreign laws and regulations** , as well as **regulatory guidance, governing the collection, use, disclosure, transfer, security and processing of** personally --- **personal** identifiable **data, such as** information of employees **that we collect about participants and healthcare providers in connection with clinical trials** . Similarly **Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future** , **which may create uncertainty in our business, affect our** our **or** third **our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, result in liability or impose additional compliance or other costs on us. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self** - party CROs, CMOs and other contractors and consultants possess certain of our sensitive data. The secure maintenance of this information is material to our operations and business strategy. Despite the implementation of security measures, our internal computer systems and those of our third- party CROs, CMOs and other contractors and consultants are vulnerable to attacks by hackers, damage from computer viruses, unauthorized access, breach due to employee error, malfeasance or other disruptions, natural disasters, terrorism and telecommunication and electrical failures. Additionally, having shifted substantially to remote working arrangements, we also face a heightened risk of cybersecurity attacks or data security incidents and are more dependent on internet and telecommunications access and capabilities. Any such attack or breach could compromise our networks and the

~~information stored there could be accessed, publicly disclosed, lost or stolen. The legislative and~~ regulatory **standards** ~~landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. Thus, any access, disclosure or other loss of information, including our data being breached at our partners or third- party providers,~~ could result in ~~legal claims or~~ **negative publicity, diversion of management time and effort and** proceedings **against us by governmental entities or others. In the U. S., HIPAA, as amended by the Health Information Technology for Economic** and ~~liability under laws that protect~~ **Clinical Health Act of 2009, and regulations implemented thereunder, imposes, among other things, certain standards relating to** the privacy **, security, transmission and breach reporting** of ~~personal~~ **individually identifiable health** information ~~, disruption of our operations, and damage to our reputation,~~ **. We may obtain health information from third parties (including research institutions from** which ~~could adversely affect our business. 63 While~~ we **obtain** ~~have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of~~ clinical trial data **)** ~~for fasedienol, ituruone, AV- 101 or other product candidates could result in substantial delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent~~ that ~~any disruption or~~ **are subject to privacy and** security **requirements under HIPAA. Depending on** ~~breach results in a loss of or damage to our data or applications or other~~ -- **the facts** ~~data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities~~ and **circumstances, we** ~~the further development of our product candidates~~ could be **subject to** ~~delayed. Remote working arrangements could significantly~~ -- **significant** ~~increase the Company' s digital~~ **penalties if we violate HIPAA. Certain states have also adopted comparable privacy** and ~~cybersecurity~~ ----- **security laws** ~~risks. Most of our employees are geographically dispersed from our headquarters facility in South San Francisco~~ and **regulations** ~~now routinely work remotely. With the continuing shift to remote working~~ , ~~and~~ **which govern** the **privacy** ~~use of virtual board and executive management meetings~~ , **processing and protection** ~~cybersecurity risks are exponentially greater, including increased risk~~ of ~~phishing~~ **health- related** and other **personal information. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act of 2018 (CCPA) went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and** ~~cybersecurity~~ ---- **security** ~~attacks~~ **obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations,** as well as **a private right of action for data breaches that has** increased **the likelihood of, and risks associated with data breach litigation. Further, the California Privacy Rights Act (CPRA) generally went into effect on January 1, 2023, and significantly amends the CCPA. It imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher** risk **data, and opt outs for certain uses** of **sensitive data. It also created a new California data protection agency** ~~unauthorized~~ -- **authorized** ~~dissemination~~ **to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may also be required. Other states have enacted similar consumer privacy laws that grant rights to data subjects and place privacy and security obligations on entities handling personal data** of **consumers or households. While we are not currently subject to laws such as the CCPA, such state privacy laws and similar legislation proposed at the state and federal level could mark the beginning of a trend toward more stringent privacy legislation in the U. S., which could increase our potential liability and adversely affect our business. In addition to our operations in the U. S., which may be subject to healthcare and other laws relating to the privacy and security of health information and other personal information, we may seek to conduct future clinical trials in the United Kingdom or the European Economic Area (the EEA) and may become subject to additional European data privacy laws, regulations and guidelines. We will be subject to the data protection laws of the European Union and United Kingdom in relation to personal data we collect from these territories. These laws impose additional obligations and risk upon our business, including substantial expenses and changes to business operations that are required to comply with these laws. For example, the European Union General Data Protection Regulation (EU GDPR) went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA or in the context of our activities within the EEA. Companies that must comply with the EU GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater. In addition, some of the personal data we process in respect of clinical trial participants is special category or** sensitive personal **data under the EU GDPR** ~~information or proprietary or confidential information about us or our customers~~ , ~~employees, or business partners~~ **and subject to additional compliance obligations and to local law derogations** . ~~Despite our cybersecurity measures~~ **Since the beginning of 2021** , **after the end of the transition period following the withdrawal of the United Kingdom from the EU (Brexit),** we may **also** be **subject** ~~more susceptible~~ to ~~security breaches and other~~ -- **the United Kingdom General Data Protection Regulation** ~~security incidents because we have less capability to implement, monitor,~~ and ~~enforce~~ **Data Protection Act 2018 (collectively, the UK GDPR) which imposes separate but similar obligations to those under the EU GDPR and comparable penalties, including fines of up to £ 17. 5 million** ~~our~~ - **or** ~~information security and~~ **4 % of a noncompliant company' s global annual revenue for the preceding financial year, whichever is greater. The subsequent separation of the** data protection ~~policies. Techniques~~ **regimes of these territories mean we are required to comply with separate data protection laws in the European Union and United Kingdom, which may lead to additional compliance costs and could increase** ~~or our~~ **overall risk. The EU** ~~software used to gain unauthorized access,~~ and **UK GDPR (collectively, the GDPR),**

which deals with the processing of personal data and on the free movement of such data, imposes a broad range of strict requirements, including requirements relating to having lawful bases for processing personal data and transferring such information outside the EEA / **UK** ~~or disable~~ , **including** ~~degrade, or harm our systems may be difficult~~ to **the U. S.** ~~detect for prolonged periods of time~~ , **providing details** ~~and we may be unable~~ to ~~anticipate these~~ **those individuals regarding** ~~techniques or put in place protective or preventive measures. The damage or disruption of our systems, or the theft~~ -- **the processing** ~~or compromise~~ of **their personal** ~~our technology,~~ data, ~~or intellectual property~~ **keeping personal data secure** , **having data processing agreements** ~~may negatively impact our business, financial condition and results of operations, reputation, stock price and long- term value, which could adversely affect our Company' s business. We may acquire businesses or product candidates, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions. We may acquire additional businesses or CNS product candidates, form strategic alliances, or create joint ventures~~ with third parties **who process personal data, responding to individuals' requests to exercise their rights in respect of their personal data, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments and record- keeping. In addition to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease / change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and / or civil claims (including class actions). The GDPR imposes strict rules on the transfer of personal data out of the EEA / UK to countries not regarded by European Commission and the United Kingdom government as providing adequate protection, or the third countries, including the U. S. and the efficacy and longevity of current transfer mechanisms between the European Economic Area (the EEA) and the U. S. remains uncertain. Case law from the Court of Justice of the European Union (CJEU) states** that **reliance on the standard contractual clauses- a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism- alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case- by- case basis. On October 7, 2022, President Biden signed an Executive Order on ' Enhancing Safeguards for U. S. Intelligence Activities' which introduced new redress mechanisms and binding safeguards to address the concerns raised by the CJEU in relation to data transfers from the EEA to the U. S. and which formed the basis of the new EU- US Data Privacy Framework (DPF), as released on December 13, 2022. The European Commission adopted its Adequacy Decision in relation to the DPF on July 10, 2023, rendering the DPF effective as a EU GDPR transfer mechanism to U. S. entities self- certified under the DPF. The DPF also introduced a new redress mechanism for EU citizens which addresses a key concern in the previous CJEU judgments and may mean transfers under standard contractual clauses are less likely to be challenged in future. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a UK GDPR data transfer mechanism to U. S. entities self- certified under the UK Extension to the DPF. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular,** we ~~believe~~ **expect the DPF Adequacy Decision to be challenged and international transfers to the U. S. and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and we** will **have to** ~~complement~~ **implement revised standard contractual clauses and other relevant documentation** ~~or~~ **for** ~~augment our~~ existing **data transfers** ~~business. If we acquire businesses with~~ **within** ~~promising markets~~ **required time frames. This may lead to additional compliance costs and could increase** ~~or~~ **our** ~~technologies,~~ **overall risk. Should** we **conduct future clinical trials in** ~~may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them~~ - **the** ~~with~~ **U. K.** ~~our~~ - **or European Union** ~~existing operations and company culture. We may encounter numerous difficulties in developing~~ , **we** ~~manufacturing and marketing any new product candidates resulting from a strategic alliance, licensing transaction or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We~~ cannot assure you that ~~, following~~ **our efforts to comply with** any **obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any** such ~~acquisition~~ **investigation or charges by European data protection authorities could have a negative effect on** ~~or~~ **our** ~~licensing transaction,~~ **reputation and materially harm our business. As** we ~~will achieve~~ **continue to expand into** ~~the~~ **other** ~~expected synergies~~ **foreign countries and jurisdictions, we may be subject** to ~~justify the transaction~~ **additional laws and regulations that may affect how we conduct business** . ~~Current politics in~~ **Additional laws and regulations governing international operations could negatively impact or restrict our operations. If we expand our operations outside of** the U. S. ~~could diminish the~~ **, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The FCPA prohibits any U. S. individual or business from paying, offering, authorizing payment or offering anything of** value **, directly or indirectly, to any foreign official, political party or candidate for the purpose** of ~~value,directly or indirectly,to any foreign official,political party,or candidate for the purpose of~~ influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business.The FCPA ~~has been applied to the marketing of drugs and the conduct of clinical trials outside the U.S.The FCPA~~ also obligates companies whose securities are listed in the U.S.to comply with **certain** accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation,including international subsidiaries,and to devise and **maintain an adequate system of internal accounting controls for international operations.Compliance with the FCPA is expensive and difficult,particularly in countries in which corruption is a recognized problem.In addition,the FCPA presents particular challenges in** the pharmaceutical industry, ~~thereby diminishing~~ **because, in many countries, hospitals are operated by the government, and doctors and** ~~the~~ **other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Various laws, regulations and executive orders also restrict the use and dissemination outside of the U. S., or the**

sharing with certain non- U. S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the U. S., it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain products and product candidates outside of the U. S., which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U. S. exchanges for violations of the FCPA' s accounting provisions. We are subject to certain U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations. Among other matters, U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, corrupt or improper payments or anything else of value ~~of~~ **to** ~~our~~ **or from recipients** ~~securities. The current political environment~~ in **the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and** ~~the~~ **other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities and other organizations. We also expect our non-** U. S. **activities** ~~has led many incumbents and political candidates~~ to ~~propose various measures~~ **increase in time. We plan** to ~~reduce the~~ **engage third** ~~prices~~ **parties** for ~~pharmaceuticals. These proposals may receive increasing publicity which~~ **clinical trials and / or to obtain necessary permits** , **licenses** ~~in turn~~ , ~~may cause~~ **patent registrations and** ~~the~~ **other** ~~investing public to reduce~~ **regulatory approvals and we can be held liable for the corrupt or** ~~the~~ **other** ~~perceived value~~ **illegal activities** of ~~pharmaceutical companies. Any decrease in the overall perception of the pharmaceutical industry may~~ **our personnel, agents or partners, even if we do not explicitly authorize or** have **prior knowledge of such activities** ~~an adverse impact on our share price and may limit our ability to raise capital needed to continue our drug development programs~~ . ~~64~~ Risks Related to Our Intellectual Property Rights If we are unable to adequately protect our proprietary technology or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us ~~more directly~~ , which would have a material adverse impact on our business, results of operations, financial condition and prospects. We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our product candidates, their compositions and formulations, their methods of use and methods of manufacturing, delivery devices ~~,~~ and any other inventions we consider important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our success will depend significantly on our ability to obtain and maintain **commercially meaningful** patent and other proprietary protection for commercially important technology, inventions and know- how related to our business, to defend and enforce our patents, to preserve the confidentiality of our trade secrets and to operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know- how, continuing technological innovation and in- licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates. We own patents and patent applications related to product candidates fasedienol ~~(PH94B)~~ , ituruvone ~~(PH10)~~ , PH80, PH15 **,** and AV- 101 and have licensed patents and patent applications related to certain stem cell technology. Although we own and have licensed issued and patents and pending patent applications relating to our product candidates in the U. S. and selected countries in other markets, we cannot provide any assurances that our pending U. S. and corresponding foreign patent applications will mature into issued patents and, if they do, that any of our patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. Moreover, other parties may have developed technologies that may be related or competitive to our product candidates and may have filed or may file patent applications and may have **been** granted or may be granted patents that overlap or conflict with our patent properties, for example, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third- party patent positions may limit or even eliminate our ability to obtain or maintain patent protection and may limit or eliminate our ability to commercialize our product candidates. The uncertainty about adequate protection includes changes to the patent laws through either legislative action to change statutory patent law or court action that may reinterpret existing law in ways affecting the scope or validity of issued patents. Moreover, relevant laws differ from country to country. The patent positions of biopharmaceutical companies, including our patent portfolio with respect to our product candidates, involve complex legal and factual questions, and, therefore, the issuance, scope, validity, and enforceability of any patent claims that we may be granted cannot be predicted with certainty. Our ability to obtain valid and enforceable patents depends, among other factors, on whether the differences between our technology and the prior art allow our inventions to be patentable over the relevant prior art. Such prior art includes, for example, scientific publications, investment blogs, granted patents, and published patent applications. Patent uncertainty cannot be eliminated because of the potential existence of other prior art, about which we are currently unaware, that may be relevant to our patent applications and patents and that may prevent a pending patent application from being granted or result in an issued patent being held invalid or unenforceable. Moreover, the relevant standards for granting and reviewing patents vary among the countries in which we pursue patents. In addition, some patent- related uncertainty exists because of the challenge of finding and addressing all of the relevant and material prior art in the biotechnology and pharmaceutical fields. For example, there are numerous reports in the scientific literature of compounds that target similar cellular receptors as do certain of our product candidates or that were evaluated in early (often pre- clinical) studies that did not progress to regulatory approval. ~~In addition, even some reports in the trade press and public announcements made by us before the filing date of our AV- 101 patent applications mentioned that AV- 101 was in development for certain therapeutic purposes.~~

~~For example, we published a web post on the NIH clinical trials website prior to the filing of our initial AV- 101 patent application, which describes unit doses for a then future study but does not mention the treatment of depression and does not provide any preclinical or clinical study data relating to depression or any other medical condition, disease or disorder. This post was not submitted to the United States Patent and Trademark Office (USPTO) in our two granted U. S. patents related to (i) unit dose formulations of AV- 101 effective to treat depression and (ii) methods of treating depression with AV- 101, respectively. However, it was submitted in two continuation depression- related AV- 101 patent applications that have similar claims, and the USPTO did not make further rejections based on that post.~~ Another source of uncertainty pertains to patent properties that were in- licensed by us for which prior art submissions were under the control of the licensor. We rely on these licensors to satisfy the relevant disclosure obligations. In the event any ~~previously published~~ prior art is deemed to be invalidating prior art, it may cause certain of our issued patents to be invalid and / or unenforceable, which would cause us to lose at least part, and perhaps all, of the patent protection on relevant product candidates. Such a loss of patent protection would have a material adverse impact on our business. ~~65~~ Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. The USPTO and various other foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other provisions during the patent process. There are situations in which noncompliance can result in the abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. Even if patents ~~do successfully issue~~ **are granted in the U. S. or other countries**, third parties may challenge the validity, enforceability, or scope of such issued patents or any other issued patents we own or license, which may result in such patents being narrowed, invalidated, or held unenforceable. ~~United States~~ **U. S.** and foreign patents and patent applications may be subject to various types of infringement and validity proceedings, including interference proceedings, ex parte reexamination, inter partes review proceedings, supplemental examination, and challenges in district court. Patents may be subjected to opposition, post- grant review, invalidity actions, or comparable proceedings lodged in various foreign, both national and regional, patent offices or courts. These proceedings could result in loss of ~~the~~ **a** patent or ~~denial~~ **rejection** of ~~the~~ **a** patent application or loss or reduction in the scope of one or more of the claims of the patent or patent in such a way that they no longer cover our product candidates or competitive products **of third parties**. Furthermore, though an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability, and the patent may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent is granted and is held to be valid and enforceable, competitors may be able to design around our patents, for example, by using pre- existing or newly developed technology **or non- infringing formulations, devices, or methods of their use**. Other parties may develop and obtain patent protection for more effective technologies, designs, or methods. If we or one of our licensing partners initiated legal proceedings against a third ~~–~~party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and / or unenforceable. In patent litigation in the ~~United States~~ **U. S.**, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness, and non- enablement. Grounds for unenforceability assertions include allegations that someone connected with the prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before administrative bodies in the ~~United States~~ **U. S.** or abroad, even outside the context of litigation. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business. In addition, such patent- related proceedings may be costly. Thus, any patent properties that we may own or exclusively license ultimately may not provide commercially meaningful protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market, or otherwise commercialize our product candidates. ~~66~~ We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, or former or current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the ~~United States~~ **U. S.**, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales. Our ability to enforce our patent rights also depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components or manufacturing processes that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement by a competitor' s or potential competitor' s product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time- consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits we initiate, **or in which we participate as a third party,** and the damages or other remedies awarded if we prevailed may not be commercially meaningful. In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any patents covering our product candidates are invalidated or found unenforceable, our financial position and results of operations could be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations could also be materially and adversely impacted. Overall, the degree of future protection for our proprietary rights is uncertain, and we cannot ensure that: ~~●~~ ● any granted patents related to our product candidates or any pending patent applications, if granted and challenged by others, will include or maintain claims having a scope sufficient to **protect** these product candidates or any other

products or product candidates against generic or other competition, particularly considering that any patent rights to these compounds per se have expired; • any of our pending patent applications will issue as patents at all; • we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire; • we were the first to make the inventions covered by each of our patents and pending patent applications; • we were the first to file patent applications for these inventions; • others will not develop similar or alternative technologies that do not infringe our patents; • others will not use pre- existing technology to effectively compete against us; • any of our patents, if issued, will ultimately be found to be valid and enforceable, including on the basis of prior art relating to our patent applications and patents; • **any of our U. S. patents, if issued, will be eligible for listing in the FDA' s " Approved Drug Products with Therapeutics Equivalents Evaluations " (commonly known as the Orange Book); • patents that are listed in the Orange Book may be challenged by the Federal Trade Commission or other as being listed inappropriately and subsequently removed, thereby depriving the Company of significant patent enforcement protections; •** any patents currently held or issued to us in the future will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties; • we will develop additional proprietary technologies or product candidates that are separately patentable; or • our commercial activities or products will not infringe ~~upon~~ the patents or proprietary rights of others. We also may rely upon unpatented trade secrets, unpatented know- how, and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees, collaborators, and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not discover or have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors **and we may thereby lose intellectual property protection** . ~~67~~ Third parties may initiate legal proceedings against us, alleging that we infringe their intellectual property rights, which may prevent or delay our product development efforts and stop us from commercializing candidate products or increase the costs of commercializing them if approved. Also, we may file counterclaims or initiate other legal proceedings against third parties to challenge the validity or scope of their intellectual property rights, the outcomes of which also would be uncertain and **a failure to prevail in such proceedings** could have a material adverse effect on the success of our business. We cannot assure that our business, product candidates, and proprietary methods do not or will not infringe the patents or other intellectual property rights of third parties. Third parties may initiate legal proceedings against us or our licensors or collaborators, alleging that we or our licensors or collaborators infringe their intellectual property rights. In addition, we or our licensors or collaborators may file counterclaims in such proceedings or initiate separate legal proceedings against third parties to challenge the validity or scope of their intellectual property rights, including in oppositions, interferences, reexaminations, inter partes reviews, or derivation proceedings before the ~~United States~~ **U. S.** or other jurisdictions. Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. Success also will depend on our ability to prevail in litigation if we are sued for infringement or to resolve litigation matters with rights and at costs favorable to us. The biopharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies ~~infringes~~ **infringe** their patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop and, if approved, commercialize our current product candidates and future product candidates, competitors may claim that our technology infringes their intellectual property rights as part of their business strategies designed to impede our successful commercialization. There may be third- party patents or patent applications with claims to materials, formulations, **devices,** methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications that later result in issued patents that our product candidates may infringe, or that such third parties assert are infringed by our technologies. The foregoing types of proceedings can be expensive and time- consuming and many of our own or our licensors' or collaborators' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these kinds of legal actions than we or our licensors or collaborators can dedicate. Our defense of litigation or other proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, the misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the ~~United States~~ **U. S.** or the European Union. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products, or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs, and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient financial resources to bring these actions to a successful conclusion. ~~68~~ An unfavorable outcome in the foregoing kinds of proceedings could require us or our licensors or collaborators to cease using the related technology or developing or commercializing **one or more of** our product candidates or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators. 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. A finding of infringement could prevent us from commercializing our product candidates or force us

to cease some of our business operations, which could materially harm our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Patent litigation and other types of intellectual property litigation can involve complex factual and legal questions, and litigation outcomes are uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney' s fees if we are found to have willfully infringed a third party' s patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim is successfully asserted against us and we are unable to obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing **one or more** our product candidates. Patent litigation and other types of intellectual property litigation is costly and time- consuming. We may not have sufficient resources to bring these actions to a successful conclusion. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. In addition, intellectual property litigation or claims could force us to do one or more of the following: • cease developing, selling or otherwise commercializing our product candidates; • pay substantial damages for past use of the asserted intellectual property; • obtain a license from the holder of the asserted intellectual property, which license may not be available on commercially reasonable terms, if at all; and • in the case of trademark claims, redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time- consuming. Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign their intellectual property to his or her employing institution. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. ~~69~~ We do not seek to protect our intellectual property rights in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection. Filing, prosecuting, and defending patents on product candidates in all countries and jurisdictions throughout the world is prohibitively expensive, and our intellectual property rights in some countries outside the U. S. could be **absent, unavailable or** less extensive than those in the U. S., assuming that rights are obtained in the U. S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U. S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S., or from selling or importing products made using our inventions in and into the U. S. or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority filing date of each of our patent applications and the time periods allowed for filing related applications in a given country. Thus, for each of the patent families that we believe provide coverage for our lead product candidates or technologies, we **must** ~~will need to~~ decide where and when to pursue protection outside the U. S. Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U. S. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U. S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology and pharmaceuticals. This could make it difficult for us to stop the infringement of our patents if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties under certain circumstances. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country- by- country basis, which is an expensive and time- consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. An unfavorable outcome could require us or our licensors or collaborators to cease using the related technology or developing or commercializing our product candidates, or to attempt to license rights to it from the prevailing party. Our business could be

harmed if the prevailing party does not offer us or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators. 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. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. ~~70~~ Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights in relevant foreign jurisdictions may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license ~~. We are dependent, in part, on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates if approved. If we breach any of the agreements under which we license the use, development, and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development or payment deadlines, we could lose license rights that are important to our business. For certain stem cell technologies, we are a party to a number of license agreements under which we are granted rights to intellectual properties that are or could become important to our business. Our existing license agreements impose, and we expect that any future license agreements will impose on us, various development, regulatory, and / or commercial diligence obligations, payment of fees, milestones and / or royalties, and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to develop or market products, which could be covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. As we have done previously, we may need to obtain licenses from third parties to advance our research or allow the commercialization of our product candidates, and we cannot provide any assurances that third- party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business, and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including: ● the scope of rights granted under the license agreement and other interpretation- related issues; ● whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; ● our right to sublicense patent and other rights to third parties under collaborative development relationships; ● our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and ● the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners. 71 If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We have entered into several licenses, both in- license agreements and out- license agreements, to support and leverage our various stem cell technology- related programs. We may enter into additional license (s) to third- party intellectual property that are necessary or useful to our business. Our current licenses, and any future licenses that we may enter into, impose various royalty payments, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, our licensor (s) may allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensor (s) may decide to terminate our license at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize a product candidate or product, if approved, as well as harm our competitive business position and our business prospects. In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms our business could suffer~~ . Some intellectual property that we have licensed may have been discovered through government- funded programs and thus may be subject to federal regulations such as " march- in " rights, certain reporting requirements, and a preference for U. S. industry. Compliance with such regulations may limit our exclusive rights, subject us to an expenditure of resources with respect to reporting requirements and limit our ability to contract with non- U. S. manufacturers. Some of the intellectual property rights we have licensed or will license in the future may have been generated through the use of U. S. government funding and may therefore be subject to certain federal regulations. As a result, the U. S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh- Dole Act ~~of 1980 (Bayh- Dole Act)~~ . These U. S. government rights in certain inventions developed under a government- funded program

include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right to require us to grant exclusive, partially exclusive, or non- exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as " march- in rights "). The U. S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Also, the U. S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government **-** funded program is further subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U. S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially **in the U. S. to the extent they are commercialized** in the U. S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U. S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U. S. manufacturers may limit our ability to contract with non- U. S. product manufacturers for products covered by such intellectual property. In the event that we apply for additional U. S. government funding **,** and we discover compounds or drug candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh- Dole Act. ~~72~~ If we do not obtain additional protection under the Hatch- Waxman Amendments and similar foreign legislation by extending the patent terms ~~and~~ **or** obtaining **regulatory and** data exclusivity for our product candidates, our business may be materially harmed. In the U. S., depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U. S. patents we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension if the active ingredient of ~~PH94B~~ **fasedienol** , ~~PH10~~ **itruvone,** or AV- 101 is used in another drug company' s product candidate and that product candidate is the first to obtain FDA approval. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected. Similar kinds of patent term and regulatory and data protection periods are available outside of the U. S. We will pursue such opportunities to extend the exclusivity of our products, but we cannot predict the availability of such exclusivity pathways or that we will be successful in pursuing them. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other pharmaceutical and biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry ~~involve~~ **involves** both technological and legal complexity and is **,** therefore **,** costly, time- consuming, and inherently uncertain. In addition, the U. S., in recent years, enacted and is currently implementing wide- ranging patent reform legislation: the Leahy- Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition. In addition, recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. The full impact of these decisions is not yet known. For example, on March 20, 2012, in Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc., the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps, and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013 **,** in Association for Molecular Pathology v. Myriad Genetics, Inc., the Court held that claims to isolated genomic DNA are not patentable but claims to complementary DNA molecules are patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. Additionally, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena, or natural products under the Myriad and Prometheus decisions. This guidance did not limit the application of Myriad to DNA but, rather, applied the decision to other natural products. Further, in 2015, in Ariosa Diagnostics, Inc. v. Sequenom, Inc., the Court of Appeals for the Federal Circuit held that methods for detecting fetal genetic defects were not patent- eligible subject matter. Other more recent court decisions and related USPTO examination guidelines must be considered, particularly as they relate to changes in what types of inventions are eligible for patent protection. Foreign patent and intellectual property laws are also evolving and are not predictable as to their impact on the Company and other biopharmaceutical companies. In addition to increasing uncertainty regarding our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions 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 any patents that may issue in the future. ~~73~~ We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers. Certain of our current employees have been, and certain of our future employees may have been, previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities. Although we are not aware of any claims currently pending or threatened against us, we may be subject to claims that we or our employees, advisors, or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or another third party. We have and may in the future also be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person' s obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail to defend such claims, in addition to paying monetary claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would materially adversely affect our commercial development efforts. Numerous factors may limit any potential competitive advantage provided by our intellectual property rights. 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, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative: ~~●~~ ~~•~~ others may be able to develop and / or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of patents, should such patents issue from our patent applications; ~~●~~ ~~•~~ we might not have been the first to make the inventions covered by a pending patent application that we own; ~~●~~ ~~•~~ we might not have been the first to file patent applications covering an invention; ~~●~~ ~~•~~ others may independently develop similar or alternative technologies without infringing our intellectual property rights; ~~●~~ ~~•~~ pending patent applications that we own or license may not lead to issued patents ~~•~~ ; ~~●~~ patents, if issued, that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable or be narrowed, as a result of legal challenges by our competitors; ~~●~~ ~~•~~ third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection; ~~●~~ ~~•~~ we may not be able to obtain and / or maintain necessary or useful licenses on reasonable terms or at all; and ~~●~~ ~~•~~ the patents of others may have an adverse effect on our business. Should any of these events occur, they could significantly harm our business and results of operations. ~~74~~ Risks Related to our Securities ~~If we fail to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted. On September 6, 2022, we were notified by the Nasdaq Stock Market, LLC (Nasdaq) that we were not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550 (a) (2) for continued listing on the Nasdaq Capital Market. Nasdaq Listing Rule 5550 (a) (2) requires listed securities to maintain a minimum bid price of $ 1. 00 per share, and Nasdaq Listing Rule 5810 (c) (3) (A) provides that a failure to meet the minimum bid price requirement exists if the deficiency continues for a period of 30 consecutive business days. The notification provided that we had 180 calendar days, or until March 6, 2023, to regain compliance with Nasdaq Listing Rule 5550 (a) (2). To regain compliance, the bid price of our common stock must have a closing bid price of at least $ 1. 00 per share for a minimum of 10 consecutive business days. Based on our written notification to Nasdaq of our intention to cure the deficiency by implementing a previously stockholder- authorized reverse stock split, if necessary, on March 7, 2023, Nasdaq granted us a second 180- day period, through September 5, 2023, in which to regain compliance. On June 6, 2023, we effected a one- for- thirty reverse split of our issued and outstanding common stock which caused the trading price of our common stock to regain compliance with the minimum bid price rule as of June 21, 2023. Although we are currently in compliance with Nasdaq' s continued listing standards, no assurance can be given that we will continue to meet applicable Nasdaq continued listing standards. Failure to meet applicable Nasdaq continued listing standards could result in a delisting of our common stock, which could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the inability to advance our drug development programs, potential loss of confidence by investors and employees, and fewer business development opportunities.~~ Market volatility may affect our stock price and the value of your investment. The market price for our common stock, similar to that of other biopharmaceutical companies, is likely to remain highly volatile. The market price of our common stock may fluctuate significantly **for no apparent reason or** in response to a number of factors, most of which we cannot control, including, among others: ~~●~~ ~~•~~ volatility resulting from uncertainty and general economic conditions; ~~●~~ ~~•~~ plans for, progress of or results from nonclinical and clinical development activities related to our product candidates; ~~●~~ ~~•~~ the failure of the FDA or other regulatory authority to approve our product candidates; ~~●~~ ~~•~~ announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors; ~~●~~ ~~•~~ the success or failure of other ~~CNS~~ **neuroscience** therapies; ~~●~~ ~~•~~ regulatory or legal developments in the U. S. and other countries; ~~●~~ ~~•~~ announcements regarding our intellectual property portfolio; ~~•~~ ~~75~~ ~~●~~ failure of our product candidates, if approved, to achieve commercial success; ~~●~~ ~~•~~ fluctuations in stock market prices and trading volumes of similar companies; ~~●~~ ~~•~~ general market conditions and overall fluctuations in U. S. equity markets; ~~●~~ ~~•~~ variations in our quarterly operating results; ~~●~~ ~~•~~ changes in our financial guidance or securities analysts' estimates of our financial performance; ~~●~~ ~~•~~ changes in accounting principles; ~~●~~ ~~•~~ our ability to raise additional capital and the terms on which we can raise it; ~~●~~ ~~•~~ sales or purchases of large blocks of our common stock, including sales or purchases by our executive officers, directors and significant stockholders; ~~●~~ ~~•~~ establishment of short positions

by holders or non- holders of our stock or warrants; • • additions or departures of key personnel; • • discussion of us or our stock price by the press and by online investor communities; and • • other risks and uncertainties described in these risk factors. ~~Future sales and issuances of our common stock may cause our stock price to decline. Sales or issuances of a substantial number of shares of our common stock in the public market, or the perception that such sales or issuances are occurring or might occur, including under our Sales Agreement, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities. The stock market in general, and small biopharmaceutical companies like ours in particular, have frequently experienced significant volatility in the market prices for securities that often has been unrelated to the operating performance of the underlying companies. These~~ **There** ~~broad market and industry fluctuations~~ may ~~adversely affect the market price of our common stock, regardless of our actual operating performance. In certain situations in which the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could~~ be **future** ~~costly and divert the time and attention of our management and harm our operating results. Additionally, if the trading volume of our common stock remains low and limited there will be an increased level of volatility and you may not be able to generate a return on your investment. If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline. The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of our common stock could decline if one or more equity research analysts downgrade our common stock or if such analysts issue other unfavorable commentary or cease publishing reports about us or our business. 76 There may be additional~~ issuances of shares of preferred stock in the future. Our Restated Articles of Incorporation, as amended (the Articles), permit us to issue up to 10. 0 million shares of preferred stock. As a result, our Board could authorize the issuance of ~~additional series of~~ preferred stock in the ~~futures~~ - **future** and such preferred stock could grant holders preferred rights to our assets upon liquidation, the right to receive dividends before dividends would be declared to holders of our common stock, and the right to the redemption of such shares, possibly together with a premium, prior to the redemption of the common stock. In the event and to the extent that we do issue additional preferred stock in the future, the rights of holders of our common stock could be impaired thereby, including without limitation, with respect to liquidation. We ~~do not intend to pay dividends on our common stock and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock. We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders purchased them. We~~ incur significant costs to ensure compliance with corporate governance, federal securities law and accounting requirements. We are subject to the reporting requirements of the ~~Securities~~ Exchange Act ~~of 1934, as amended (Exchange Act),~~ which requires that we file annual, quarterly and current reports with respect to our business and financial condition, and the rules and regulations implemented by the SEC, the Sarbanes- Oxley Act of ~~2002~~ **2022 , as amended (the Sarbanes- Oxley Act)** , the Dodd- Frank Act, and the Public Company Accounting Oversight Board, each of which imposes additional reporting and other obligations on public companies. We have incurred and will continue to incur significant costs to comply with these public company reporting requirements, including accounting and related audit costs, legal costs to comply with corporate governance requirements and other costs of operating as a public company. These legal and financial compliance costs will continue to require us to divert significant resources that we could otherwise use to achieve our research and development and other strategic objectives. The filing and internal control reporting requirements imposed by federal securities laws, rules and regulations on companies that are not " smaller reporting companies " under federal securities laws are rigorous and, once we are no longer a smaller reporting company, we may not be able to meet them, resulting in a possible decline in the price of our common stock and our inability to obtain future financing. Certain of these requirements may require us to carry out activities we have not done previously and complying with such requirements may divert management' s attention from other business concerns, which could have a material adverse effect on our business, results of operations, financial condition and cash flows. Any failure to adequately comply with applicable federal securities laws, rules or regulations could subject us to fines or regulatory actions, which may materially adversely affect our business, results of operations and financial condition. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We will continue to invest resources to comply with evolving laws, regulations and standards, however this investment may result in increased general and administrative expense **,** and a diversion of management' s time and attention from revenue- generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us **,** and our business may be adversely affected. **The amount of our future losses is uncertain and our quarterly and annual operating results may fluctuate significantly or fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following: • the timing and success or**

failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, • our ability to successfully recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts; • the risk / benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates; • our ability to obtain marketing approval for our product candidates and the timing and scope of any such approvals we may receive; • the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time; • the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers; • our ability to attract, hire and retain qualified personnel; • expenditures that we will or may incur to develop additional product candidates; • the level of demand for our product candidates should they receive approval, which may vary significantly; • the changing and volatile U. S. and global economic environments, including the impact of inflation and rising interest rates, and domestic or international political instability; and • future accounting pronouncements or changes in our accounting policies. The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period- to- period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our operating results or revenue fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide. Because of potential volatility in our trading price and trading volume, we may incur significant costs from class action securities litigation. The stock market in general, and the Nasdaq Stock Market (Nasdaq) and biotechnology and pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Historically, securities class action litigation has often been brought against companies following periods of volatility in the market price of a company' s securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management' s attention and resources, which could harm our business, operating results, or financial condition. Additionally, the dramatic increase in the cost of directors' and officers' liability insurance may cause us to opt for lower overall policy limits or to forgo insurance that we may otherwise rely on to cover significant defense costs, settlements, and damages awarded to plaintiffs. Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders. We expect to issue additional capital stock in the future that will result in dilution to all other stockholders. We expect to grant equity awards to employees and directors under our stock incentive plans. We may also raise capital through equity financings in the future. As part of our business strategy, we may acquire or make investments in complementary companies, products, or technologies and issue equity securities to pay for any such acquisition or investment. Any such issuances of additional capital stock may cause stockholders to experience significant dilution of their ownership interests and the per share value of our common stock to decline. Because we have no current plans to pay cash dividends on our common stock, you may not receive any return on investment unless you sell your common stock for a price greater than that which you paid for it. We have never declared or paid any cash dividends on our capital stock and have no current plans to pay cash dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions, and other factors that our board of directors may deem relevant. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Future offerings of debt or equity securities by us may adversely affect the market price of our common stock. In the future, we may attempt to obtain financing or to further increase our capital resources by issuing additional shares of our common stock or offering debt or other equity securities, including commercial paper, medium- term notes, senior or subordinated notes, debt securities convertible into equity or shares of preferred stock. Future acquisitions could require substantial additional capital in excess of cash from operations. We would expect to obtain the capital required for acquisitions through a combination of additional issuances of equity, corporate indebtedness and / or cash from operations. Issuing additional shares of our common stock or other equity securities or securities convertible into equity may dilute the economic and voting rights of our existing stockholders or reduce the market price of our common stock or both. Upon liquidation, holders of such debt securities and preferred shares, if issued, and lenders with respect to other borrowings would receive a distribution of our available assets prior to the holders of our common stock. Debt securities convertible into equity could be subject to adjustments in the conversion ratio pursuant to which certain events may increase the number of equity securities issuable upon conversion. Preferred shares, if issued, could have a preference with respect to liquidating distributions or a preference with respect to dividend payments that could limit our ability to pay dividends to the holders of our common stock. Our decision to issue securities in any future offering will depend on market conditions and other factors beyond our control, which may adversely affect the amount, timing and nature of our future offerings. General Risk Factors Adverse market or macroeconomic conditions or market volatility resulting from global economic developments, including those affecting the financial services industry, could adversely affect our business operations and our financial condition and results of operations. Adverse market or macroeconomic conditions or market volatility resulting from global economic developments, political unrest, high inflation, rising interest rates, the post- COVID environment or other factors, could materially and adversely affect our business operations. For instance, actual events involving limited liquidity, defaults, non- performance or other adverse

developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market- wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (the FDIC) as receiver. Similarly, on March 12, 2023, Signature Bank Corp. and Silvergate Capital Corp. were each swept into receivership, and uncertainty remains over liquidity concerns in the broader financial services industry. We may maintain cash balances at third- party financial institutions in excess of the FDIC standard insurance limit. Although the U. S. Department of Treasury, FDIC and Federal Reserve Board announced a program to provide up to $ 25. 0 billion of loans to financial institutions secured by certain of such government securities held by financial institutions, widespread demands for customer withdrawals or other liquidity needs of financial institutions may exceed the capacity of such program, and there is no guarantee that the U. S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of such banks or financial institutions, or that they would do so in a timely fashion. These events could result in a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations, including, but not limited to, the following: • delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets; • potential or actual breach of statutory, regulatory or contractual obligations, including obligations that require us to maintain letters of credit or other credit support arrangements; or • termination of cash management arrangements and / or delays in accessing or actual loss of funds subject to cash management arrangements. In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our partners, vendors or suppliers, which in turn, could have a material adverse effect on our current and / or projected business operations and results of operations and financial condition. For example, a partner may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition, a vendor or supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that could result in material adverse impacts on us, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. The bankruptcy or insolvency of any partner, vendor or supplier, or the failure of any partner to make payments when due, or any breach or default by a partner, vendor or supplier, or the loss of any significant supplier relationships, could cause us to suffer material losses and may have a material adverse impact on our business. Changes in tax law could adversely affect our business and financial condition. The rules dealing with U. S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application), including with respect to net operating losses and research and development tax credits, could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock. Our ability to use our net operating losses and research and development tax credits to offset future taxable income may be subject to certain limitations. As of March 31, 2024, we had U. S. federal net operating loss carryforwards totaling $ 208. 0 million, all of which have an indefinite carryforward period. Federal net operating loss carryforwards of approximately $ 82. 8 million generated through our fiscal year ended March 31, 2018 will expire in our fiscal years ending March 31, 2025 through March 31, 2038. Federal net operating loss carryforwards of approximately $ 125. 2 million generated in fiscal years ending after March 31, 2018 will carry forward indefinitely. As of March 31, 2024, we had state net operating loss carryforwards totaling $ 65. 8 million, which expire at various dates between 2029 and 2044. As of March 31, 2024, we also had U. S. federal and state research and development tax credit carryforwards of $ 3. 3 million and $ 1. 6 million, respectively, which begin to expire in 2029 for federal purposes, state credits do no expire. The net operating losses which are limited in life and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) a corporation that undergoes an " ownership change " is subject to limitations on its ability to utilize its pre- change net operating losses (NOLs) or tax credits or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who own at least 5 % of a corporation' s stock increase their ownership by more than 50 percentage points over their lowest ownership percentage within a specified testing period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in the future, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. If we determine that an ownership change has occurred and our ability to use our historical NOLs or credits is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. Section 382 and 383 of the Code would apply to all net operating loss and tax credit carryforwards, whether the carryforward period is indefinite or not. Furthermore, our ability to utilize our historical NOLs or credits is conditioned upon us attaining profitability and generating U. S. federal and state taxable income. We are a clinical- stage biopharmaceutical company with a limited operating history. We have incurred significant net losses

since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; and therefore, we do not know whether or when we will generate the U. S. federal or state taxable income necessary to utilize our historical NOLs or credits that may be subject to limitation by Sections 382 and 383 of the Code. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected. If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing we conduct in connection with Section 404 of the Sarbanes- Oxley Act of 2022, as amended (the Sarbanes- Oxley Act), or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock. If we identify any future material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports or applicable stock exchange listing requirements, investors may lose confidence in our financial reporting and our stock price may decline as a result. We also could become subject to investigations by Nasdaq, the SEC or other regulatory authorities. Reports published by analysts, including projections in those reports that differ from our actual results, could adversely affect the price and trading volume of our common stock. Securities research analysts may establish and publish their own periodic projections for us. These projections may vary widely and may not accurately predict the results we actually achieve. Our share price may decline if our actual results do not match the projections of these securities research analysts. Similarly, if one or more of the analysts who write reports on us downgrades our stock or publishes inaccurate or unfavorable research about our business, our share price could decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, our share price or trading volume could decline. There can be no assurance that we will be able to comply with the continued listing standards of Nasdaq. If Nasdaq delists our shares of common stock from trading on its exchange for failure to meet Nasdaq' s listing standards, we and our stockholders could face significant material adverse consequences including: • a limited availability of market quotations for our securities; • reduced liquidity for our securities; • a determination that our common stock is a " penny stock " which will require brokers trading in our common stock to adhere to more stringent rules and possibly result in a reduced level of trading activity in the secondary trading market for our securities; • a limited amount of news and analyst coverage; and • a decreased ability to issue additional securities or obtain additional financing in the future. The price of our common stock may be volatile. The price of our common stock may fluctuate due to a variety of factors, including: • changes in the industries in which we and our customers operate; • variations in our operating performance and the performance of our competitors in general; • material and adverse impact of the COVID- 19 pandemic and post- COVID environment on the markets and the broader global economy; • actual or anticipated fluctuations in our quarterly or annual operating results; • publication of research reports by securities analysts about us, our competitors or our industry; • the public' s reaction to our press releases, other public announcements and filings with the SEC; • our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market; • additions and departures of key personnel; • changes in laws and regulations affecting our business; • commencement of, or involvement in, litigation involving us; • changes in our capital structure, such as future issuances of securities or the incurrence of additional debt; • the volume of shares of our common stock available for public sale; and • general economic and political conditions such as recessions, rising interest rates, inflation, fuel prices, foreign currency fluctuations, international tariffs, boycotts, curtailment of trade and other business restrictions, social, political and economic risks, natural disasters and acts of war or terrorism, such as the conflicts involving Ukraine and Russia, or Israel and its surrounding regions. These market and industry factors may materially reduce the market price of shares of our common stock regardless of our operating performance.