Risk Factors Comparison 2024-03-19 to 2023-03-23 Form: 10-K

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

This section provides a summary of the risks that may impact our performance in the future. For details of our various risk factors and their impacts, see " Risk Factors Discussion. " Our risk factors are organized into the following categories: 1) Risks related to our business, 2) Risks related to clinical and regulatory matters, 3) Risks related to our intellectual property, 4) Risks related to government regulations, 5) Risks related to our reliance on third parties, and 6) Risks related to ownership of our common stock. Business risks include risks associated with our products and regulatory approval, licensing agreements, historical losses, managing growth, **and** acquisitions ~~, the COVID- 19 pandemic, and Russia' s Invasion of Ukraine~~ . In general, the risks related to our business can cause variability in the future profits of the Company. **Risks related to clinical and regulatory matters** Clinical and regulatory matters include risks associated with clinical trials and the future ability to commercially market the product. In order for any of our products to be commercialized and produce future profits, successful trials need to be completed with supporting data to receive regulatory approval. Failing to complete the trial will significantly increase our cost of doing business. In addition, the active ingredient in our products is a controlled substance which can affect the supply available for clinical trials, as well as commercial sales. A limited supply could increase the time needed to complete clinical trials and overall costs including product liability claims. We could also face potential fines or reputational risk if we do not comply. Developments from competitors and the ability to obtain market exclusivity could also negatively impact future profits. Risks related to our intellectual property Our products depend upon securing and protecting critical intellectual property. Patent positions are highly uncertain and involve complex legal and factual questions. Infringing upon patents or trade secrets could force us to cease or alter our product development efforts or obtain a license to continue to develop or sale our products. These risks could not only impact the future profits of the company but also create adverse publicity for us. We are required to comply with various federal and state pharmaceutical and healthcare laws and regulations, and to maintain secure systems to protect sensitive confidential information. Complying with the various regulations can increase our cost of doing business. We could also face potential fines or reputational risk if we do not comply. Litigation or investigations can increase costs, negatively affect our operating results and create adverse publicity for us. The Company relies on third parties to conduct preclinical and clinical studies, as well as to manufacture our product candidates. Third parties' failure to perform the trials as contractually required could impact our ability to obtain regulatory approval. If our third- party manufacturers fail to meet our requirements and strict regulatory requirements, our product development and commercialization efforts may be materially harmed. Risks related to ownership of our common stock Common stocks risks include risks associated with the limited market for our common stock, a potential issuance of a substantial number of additional shares, stock price volatility, and reporting requirements of federal securities laws. The net effect of these risks can include reductions in future profits, additional operating expenses, inability to meet liquidity needs, inability to access capital and increased cost of capital. Risks Related to Our Business Our business depends on the success of esmethadone (d- methadone, dextromethadone, REL- 1017), our only product candidate currently in clinical development, which is in a pivotal clinical ~~trials~~ **trial** for the adjunctive treatment of MDD. If we are unable to obtain regulatory approval for and successfully commercialize REL- 1017 or other future product candidates, or we experience significant delays in doing so, our business will be materially harmed. To date, the primary focus of our product development has been esmethadone (d- methadone, dextromethadone, REL- 1017) for the adjunctive ~~and monotherapy~~ treatment of patients with MDD. Currently, esmethadone is our only product candidate under clinical development **. We intend, in 2024, to enter human studies of our proprietary, low dose modified- release formulation of psilocybin (REL- P11) for metabolic indications, but there can be no assurance that such studies will be commenced or completed** . This may make an investment in our Company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a setback of a lead candidate. Successful continued development and ultimate regulatory approval of esmethadone for the adjunctive treatment of MDD ~~, and potentially as a monotherapy for MDD,~~ or other indications is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the clinical development of esmethadone. If we cannot successfully develop, obtain regulatory approval for and commercialize esmethadone, we may not be able to continue our operations. The future regulatory and commercial success of esmethadone is subject to a number of risks, including the following: ● we may not be able to obtain adequate evidence from clinical trials to support the efficacy and safety for esmethadone for the adjunctive treatment of MDD ~~, monotherapy for MDD,~~ or other indications; ● we may not be able to demonstrate that the benefits of esmethadone for the adjunctive treatment of MDD ~~, monotherapy for MDD,~~ or other indications outweigh the risks; ● in our clinical trials for esmethadone, enrollment may be slower than anticipated and we may need additional clinical trial sites than originally planned, which could delay our clinical trial progress; ● the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for marketing approval; ● patients in our clinical trials may suffer serious adverse effects for reasons that may or may not be related to esmethadone, which could delay or prevent further clinical development; ● the standards implemented by clinical or regulatory agencies may change at any time and we cannot be certain what efficacy endpoints the FDA or foreign clinical or regulatory agencies may require in pivotal clinical trials with respect to the adjunctive treatment of MDD ~~, monotherapy for MDD,~~ or any other indication for the approval of esmethadone; ● the results of later stage clinical trials may not be as favorable as the results we have observed to date in our preclinical studies and Phase 1 and 2 clinical trials; ● we cannot be certain of the number and type of clinical trials and preclinical or toxicology studies that the FDA or other regulatory agencies will require in order to approve esmethadone for the

adjunctive treatment of MDD ~~, monotherapy for MDD,~~ or any other indication; ● we may not have sufficient financial and other resources to complete the necessary clinical trials for esmethadone, including, but not limited to, the clinical trials needed to obtain drug approval; ● if approved for the adjunctive treatment of MDD, ~~monotherapy for MDD,~~ esmethadone will likely compete with products that may reach approval prior to esmethadone, products that are currently approved for the adjunctive treatment of MDD ~~, monotherapy for MDD,~~ and the off- label use of currently marketed products for MDD; and ● we may not be able to obtain, maintain or enforce our patents and other intellectual property rights. Esmethadone **, psilocybin** and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and comparable foreign regulatory authorities before obtaining marketing approval **, if at all,** from these regulatory authorities ~~, if at all~~ . The drug development and approval process is lengthy and expensive, and approval is never certain. Investigational new drugs, such as esmethadone, may not prove to be safe and effective in clinical trials. We have limited experience as a company in conducting later stage clinical trials required to obtain regulatory approval. We may be unable **, if at all,** to conduct future clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion ~~, if at all~~ . In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Because we have limited experience as a company designing clinical trials, we may be unable to design and execute clinical trials to support regulatory approval. There is a high failure rate for drugs and biological products proceeding through clinical trials. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of esmethadone **, psilocybin** or any future product candidate may not be predictive of the results of later- stage clinical studies or trials and the results of studies or trials in one set of patients or line of treatment may not be predictive of those obtained in another. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in preclinical studies and earlier stage clinical trials. In addition, data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. Owing in part to the complexity of biological pathways, esmethadone **, psilocybin** or any future product candidate may not demonstrate in patients the biochemical and pharmacological properties we anticipate based on laboratory studies or earlier stage clinical trials, and they may interact with human biological systems or other drugs in unforeseen, ineffective or harmful ways. The number of patients exposed to product candidates and the average exposure time in the clinical development programs may be inadequate to detect rare adverse events or findings that may only be detected once a product candidate is administered to more patients and for greater periods of time. Our Phase 2 clinical study of REL- 1017 involved a small population of subjects with MDD, and, because of the small sample size in such trial, the results of this clinical trial may be subject to substantial variability and may not be indicative of either future top- line results or final results. **In addition, results from open- label trials, such as our open- label trial of REL- 1017, may not predict results in placebo- controlled trials for a number of reasons, including biases that may exaggerate therapeutic effect.** On October 13, 2022, we announced that the RELIANCE III study, evaluating REL- 1017 in the monotherapy setting for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the MADRS on Day 28. On December 7, 2022, we announced that the RELIANCE I study **, evaluating REL- 1017 in the adjunctive setting for MDD,** did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the MADRS on Day 28. With these findings, even if RELIANCE II **, RELIGHT,** or **any** additional Phase ~~III~~ **3** studies achieve their primary endpoints, we may not have sufficient evidence to demonstrate the efficacy of REL- 1017 as an adjunctive treatment of MDD. If we are unable to successfully demonstrate the safety and efficacy of esmethadone **, psilocybin** or other future product candidates and receive the necessary regulatory approvals, our business will be materially harmed. Even if we do receive regulatory approval to market esmethadone, **psilocybin or other future product candidates,** any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we may be unable to successfully develop or commercialize esmethadone **, psilocybin or other future product candidates** . If we or any of our future development collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize esmethadone **, psilocybin or other future product candidates** , we may not be able to generate sufficient revenue to continue our business. Preliminary or top- line results may not accurately reflect the complete results of the clinical study. Preliminary or top- line data remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or top- line data. As a result, preliminary or top- line data should be viewed with caution until the final data are available. Our license agreement for esmethadone, our only product candidate currently under clinical development, could terminate under certain circumstances, including if we terminate our Chief Executive Officer except for cause, and we would be unable to conduct our business as planned. In January 2018, we entered into an Intellectual Property Assignment Agreement (the ~~“~~ Assignment Agreement ~~”~~) and License Agreement (the License Agreement and together with the Assignment Agreement, the Agreements), with Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (collectively, the ~~“~~ Licensor ~~”~~). Pursuant to the Assignment Agreement, we assigned our existing rights, including patents and patent applications, to esmethadone in the context of psychiatric use to Licensor, and pursuant to the License Agreement, Licensor then granted us an exclusive perpetual, worldwide license under the assigned intellectual property rights as well as patents and know- how covering certain new inventions developed by Licensor and relating to esmethadone in neurological and other uses, to develop and commercialize esmethadone in all fields of use. The License Agreement also grants to us rights in all future inventions developed by Licensor, whether or not in collaboration with us that relate in any way to esmethadone or the use thereof. The License Agreement was amended in December 2019 to modify certain termination rights relating to the Chief Executive Officer, which are described further below. If we develop any new inventions relating to esmethadone, we are required to do so in collaboration with Licensor, and to file patents covering such

inventions jointly in the name of the Company and Licensor. All such future inventions or patents shall be jointly owned by us and Licensor and, will be included in and subject to the financial and other terms of the License Agreement. The License Agreement includes standard termination rights for Licensor in the event of our insolvency, challenge of the licensed patents and uncured material breach of our obligations under the License Agreement. In addition, the License Agreement contains certain " Key Man " provisions such that the Licensor may terminate the License Agreement if we terminate the employment of our Chief Executive Officer, Mr. Sergio Traversa, for any reason other than for specified causes determined by a majority of our Board of Directors (including fraud, gross negligence, unauthorized use of our confidential information, conduct including harassment or discrimination, breach of fiduciary duty or uncured material breach), or if we (a) substantially modify Mr. Traversa' s job responsibilities or decision- making rights in connection with the development and commercialization of esmethadone, (b) remove him from the role of Chief Executive Officer other than in connection with a permitted change- of- control transaction, (c) materially reduce his compensation, or (d) assign or transfer our rights under the License Agreement or the esmethadone intellectual property without Mr. Traversa' s consent, in each case (termination or the events in (a) through (d) during the period commencing on the effective date and ending on the later of five years from the original effective date of the License Agreement on December 31, 2022. The December 2019 amendment to the License Agreement made certain clarifications to the nature of a termination for Cause, including to clarify that termination due to Mr. Traversa' s death or disability does not give Licensor the right to terminate the License Agreement. On December 27, 2022, the Licensor and the Company entered into a new amendment extending the " Key Man " provision period until December 31, 2027. The License Agreement was not otherwise modified. As a result of the provisions described above, we are limited in our ability to terminate, as well as to decrease the salary or authority of, our Chief Executive Officer until December 31, 2027. In addition, the agreement provides that any assignor that we assign the agreement to must agree in writing to all terms of the license, including the key man provisions, and as noted above, our Chief Executive Officer has the right to consent to any such assignment of the agreement unless previously terminated for cause or due to death. As the license agreement relates to our only product candidate currently under clinical development, these provisions may be deemed to have an anti- takeover effect and may delay, deter or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders. If we fail to comply with the terms of the License Agreement, our rights to those patents may be terminated, and we will be unable to conduct our business. We have generated no revenue from commercial sales to date and our future profitability is uncertain. We have a limited operating history and our business is subject to all of the risks inherent in the establishment of a new business enterprise. Our likelihood of success must be considered in light of the problems, expenses, difficulties, complications and delays frequently encountered in connection with this. Since we began our business, we have focused on research, development and clinical trials of product candidates, and have incurred significant losses since inception and generated no product revenues. If we continue to incur operating losses and fail to become a profitable company, we may be unable to continue our operations. We expect to continue to operate at a net loss for at least the next several years as we continue our research and development efforts, continue to conduct clinical trials and develop manufacturing, sales, marketing and distribution capabilities. There can be no assurance that the products under development by us will be approved for sales in the US or elsewhere. Furthermore, there can be no assurance that if such products are approved they will be successfully commercialized, and the extent of our future losses and the timing of our profitability are highly uncertain. International commercialization of our product candidates faces significant obstacles. We may plan to commercialize some of our products internationally through collaborative relationships with foreign partners. We have limited foreign regulatory, clinical and commercial resources. Future partners are critical to our international success. We may not be able to enter into collaboration agreements with appropriate partners for important foreign markets on acceptable terms, or at all. Future collaborations with foreign partners may not be effective or profitable for us. We will need to obtain approvals from the appropriate regulatory, pricing and reimbursement authorities to market any of our proposed products internationally, and we may be unable to obtain foreign regulatory approvals. Pursuing foreign regulatory approvals will be time- consuming and expensive. The regulations can vary among countries and foreign regulatory authorities may require different or additional clinical trials than we conducted to obtain FDA approval for our product candidates. In addition, adverse clinical trial results, such as death or injury due to side effects, could jeopardize not only regulatory approval, but if approval is granted, may also lead to marketing restrictions. Our product candidates may also face foreign regulatory requirements applicable to controlled substances. We have a history of losses and we may never achieve or sustain profitability. We have incurred substantial losses since our inception, and we may not achieve profitability for the foreseeable future, if at all. Since inception, we have an accumulated deficit of approximately $ ~~462~~ **560** . ~~1~~ **9** million at December 31, ~~2022~~ **2023** . The Company had cash, cash equivalents and short- term investments of approximately $ ~~148~~ **96** . 3 million at December 31, ~~2022~~ **2023** . Even if we succeed in developing and commercializing one or more of our product candidates, we expect to incur substantial net losses and negative cash flows for the foreseeable future due in part to increasing research and development expenses, including clinical trials, and increasing expenses from leasing additional facilities and hiring additional personnel. As a result, we will need to generate significant revenues in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the future. Even if we do achieve profitability, we may not be able to sustain or increase profitability. We have a limited operating history upon which to base an investment decision. Our limited operating history may limit your ability to evaluate our prospects due to our limited historical financial data and our unproven potential to generate profits. You should evaluate the likelihood of financial and operational success in light of the risks, uncertainties, expenses and difficulties associated with an early- stage business, many of which may be beyond our control, including: ● our potential inability to continue to undertake preclinical studies, pharmaceutical development and clinical trials, ● our potential inability to obtain regulatory approvals, and ● our potential inability to manufacture, sell and market our products. Our operations have been limited to organizing and staffing, on a limited basis, our company, acquiring, developing and securing our proprietary

technology and undertaking preclinical studies and clinical trials of our principal product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our common stock. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. As of December 31, ~~2022~~ **2023**, we had Federal, New York State and New York City net operating loss (NOL) carryforwards of approximately $ ~~118~~ **100**, ~~877~~ **077**, 000, $ ~~74~~ **15**, ~~792~~ **016**, 000 and $ ~~74~~ **14**, ~~608~~ **998**, 000, respectively, which begin expiring in ~~2028~~ **2027**, ~~2033~~ **2032** and ~~2033~~ **2032**, respectively. Under U. S. federal tax legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, or Tax Act, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal NOLs is limited to 80 % of taxable income in the year. It is uncertain if and to what extent various states will conform to the Tax Act. Under Sections 382 and 383 of the U. S. Internal Revenue Code of 1986, as amended, if a corporation undergoes an " ownership change " (generally defined as a greater than 50 percentage- point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three- year period), the corporation' s ability to use its pre- change NOLs and other pre- change tax attributes to offset its post- change taxable income or taxes may be limited. We may also experience ownership changes as a result of stock offerings or as a result of subsequent shifts in our stock ownership, some of which are outside our control. We have not completed an analysis to determine whether any such limitations have been triggered. If any were determined to be triggered, our ability to use our current NOLs and other pre- change tax attributes to offset post- change taxable income or taxes would be subject to limitation. We will be unable to use our NOLs if we do not attain profitability sufficient to offset our available NOLs prior to their expiration. We may not be successful in hiring and retaining key employees. Our future operations and successes depend in large part upon the continued service of key members of our senior management team whom we are highly dependent upon to manage our business, specifically Dr. Sergio Traversa, our Chief Executive Officer, **and** Dr. Paolo Manfredi, Acting Chief Scientific Officer ~~, and Dr. Cedric O' Gorman, Chief Medical Officer~~. If ~~any~~ **either** terminates employment with us, such a departure would have a material adverse effect on our business. Our future success also depends on our ability to identify, attract, hire or engage, retain and motivate other well- qualified managerial, technical, clinical and regulatory personnel. We currently only have ~~14~~ **16** full time employees and are likely to hire additional qualified personnel with expertise in nonclinical pharmacology and toxicology, pharmaceutical development, clinical research, regulatory affairs, manufacturing, sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for such individuals, particularly in the United States, is intense, and we may not be able to hire sufficient personnel to support our efforts. There can be no assurance that these professionals will be available in the market, or that we will be able to retain existing professionals or to meet or to continue to meet their compensation requirements. Furthermore, the cost base in relation to such compensation, which may include equity compensation, may increase significantly, which could have a material adverse effect on us. Failure to establish and maintain an effective management team and work force could adversely affect our ability to operate, grow and manage our business. Managing our growth as we expand operations may strain our resources. We expect to need to grow rapidly in order to support ongoing and additional, larger, and potentially international, pivotal clinical trials of our drug candidates, which will place a significant strain on our financial, managerial and operational resources. In order to achieve and manage growth effectively, we must continue to improve and expand our operational and financial management capabilities. Moreover, we will need to increase staffing and to train, motivate and manage our employees. We may expand our business through the acquisition of rights to new drug candidates that could disrupt our business, harm our financial condition and may also dilute current stockholders' ownership interests in our company. Our business strategy includes expanding our products and capabilities, and we may seek acquisitions of drug candidates or technologies to do so. Acquisitions involve numerous risks, including substantial cash expenditures; potentially dilutive issuance of equity securities; incurrence of debt and contingent liabilities, some of which may be difficult or impossible to identify at the time of acquisition; difficulties in assimilating the acquired technologies or the operations of the acquired companies; diverting our management' s attention away from other business concerns; risks of entering markets in which we have limited or no direct experience; and the potential loss of our key employees or key employees of the acquired companies. We cannot assure you that any acquisition will result in short- term or long- term benefits to us. We may incorrectly judge the value or worth of an acquired product, company or business. In addition, our future success would depend in part on our ability to manage the rapid growth associated with some of these acquisitions. We cannot assure you that we will be able to make the combination of our business with that of acquired products, businesses or companies work or be successful. Furthermore, the development or expansion of our business or any acquired products, business or companies may require a substantial capital investment by us. We may not have these necessary funds or they might not be available to us on acceptable terms or at all. We may also seek to raise funds by selling shares of our preferred or common stock, which could dilute each current stockholder' s ownership interest in us. Business interruptions could limit our ability to operate our business. Our operations as well as those of our collaborators on which we depend are vulnerable to damage or interruption from computer viruses, human error, natural disasters, electrical and telecommunication failures, international acts of terror and similar events. We have not established a formal disaster recovery plan and our back- up operations and our business interruption insurance may not be adequate to compensate us for losses we may suffer. A significant business interruption could result in losses or damages incurred by us and require us to cease or curtail our operations ~~. Our business could be adversely affected by the effects of health epidemics, including the global COVID- 19 pandemic. In December 2019, a novel strain of COVID- 19 was reported in China. Since then, COVID- 19 has spread globally, to include the United States. The spread of COVID- 19 has resulted in the World Health Organization (WHO) declaring the outbreak of COVID- 19 as a " pandemic, " or a worldwide spread of a new disease, on March 11, 2020. Many countries around the world have imposed quarantines, travel restrictions, limitations on gatherings, closures of businesses and other social distancing measures. As local jurisdictions put restrictions in place, our ability to continue to operate our business may also be limited. Such events may result in a period of business and manufacturing disruption, and in reduced operations, any of which could materially affect our~~

~~business, financial condition and results of operations. The COVID- 19 pandemic and efforts to contain the outbreak have led to economic disruption, including changes in interest rates, extreme volatility in financial markets, fluctuations in foreign currency exchange rates, changes in economic activity and changes in unemployment claims. While the potential economic impact brought by COVID- 19 may be difficult to assess or predict, a more protracted pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID- 19 could materially affect our business and the value of our common shares. The continued spread of COVID- 19 globally could also adversely affect our planned clinical trial operations, including our ability to initiate trials on expected timelines and recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID- 19 if an outbreak occurs in their geography. Further, the COVID- 19 outbreak could result in delays in our clinical trials due to prioritization of hospital resources toward the outbreak, restrictions in travel, potential unwillingness of patients to enroll in trials at this time, or the inability of patients to comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services. In addition, we rely on independent clinical investigators, contract research organizations and other third- party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and an outbreak may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us. Additionally, COVID- 19 may also result in delays in receiving approvals from local and foreign regulatory authorities, delays in necessary interactions with local and foreign regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees. The global outbreak of COVID- 19 continues to evolve. The ultimate long- term impact of COVID- 19 is highly uncertain and cannot be predicted with confidence. In addition, since COVID- 19 is a pandemic, it could materially affect our operations globally, including at our headquarters and at our future clinical trial sites throughout the globe. Our business could be adversely affected by health epidemics in regions where we have significant manufacturing and distribution facilities, concentrations of clinical trial sites or other business operations. The ultimate impact of the COVID- 19 outbreak or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our supply chain, clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and, therefore, we will continue to monitor the COVID- 19 situation closely and implement risk mitigation as needed. Our business could be adversely affected by the effects of Russia' s invasion of Ukraine. On February 24, 2022, Russia launched a large- scale invasion of Ukraine. The United States and other countries and certain international organizations have imposed broad- ranging economic sanctions on Russia and certain Russian individuals, banking entities and corporations as a response, and additional sanctions may be imposed in the future. The extent and duration of the military action or future escalation of such hostilities, resulting sanctions and future market disruptions and volatility are impossible to predict, but could be significant and could have a severe adverse effect on the regional and global economies. The ramifications of the hostilities and sanctions may not be limited to Russia, Ukraine and Russian and Ukrainian companies but may spill over to and negatively impact other regional and global economic markets (including Europe and the United States), companies in other countries (particularly those that have done business with Russia and Ukraine) and on various sectors, industries and the markets for credit, securities and commodities globally. In addition, Russia may take retaliatory actions and other countermeasures, including cyberattacks and espionage against other countries and companies around the world, including attacks on key infrastructure such as the power grid and the internet. The potential for a wider conflict could further increase financial market volatility and could negatively affect our ability to raise additional capital when required. While we do not currently conduct any business in Russia or Ukraine, the conflict and its effects could adversely affect our planned clinical trial operations, including our ability to recruit and retain patients~~ . Risks Related to Clinical and Regulatory Matters If we or our potential collaborators fail to obtain the necessary regulatory approvals, or if such approvals are limited, we and our potential collaborators will not be allowed to commercialize our drug candidates, and we will not generate product revenues. Satisfaction of all regulatory requirements for commercialization of a drug candidate typically takes many years, is dependent upon the type, complexity and novelty of the drug candidate, and requires the expenditure of substantial resources for research and development. Our research and clinical approaches may not lead to drugs that the FDA considers safe for humans and effective for indicated uses we are studying. The FDA may require studies in addition to those we are conducting, in which case we or our collaborators would have to expend additional time and resources and would likely delay the date of potentially receiving regulatory approval. The approval process may also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals would: ● delay commercialization of, and product revenues from, our drug candidates; and ● diminish the competitive advantages that we may have otherwise enjoyed, which would have an adverse effect on our operating results and financial condition. Even if we or our collaborators comply with all FDA regulatory requirements, our drug candidates may never obtain regulatory approval. If we or our collaborators fail to obtain regulatory approval for any of our drug candidates we will have fewer commercial products, if any, and corresponding lower product revenues, if any. Even if our drug candidates receive regulatory approval, such approval may involve limitations on the indications and conditions of use or marketing claims for our products. Further, later discovery of previously unknown problems or adverse events could result in additional regulatory restrictions, including withdrawal of products. The FDA may also require us or our collaborators to commit to perform lengthy Phase 4 post- approval clinical efficacy or safety studies. Our expending additional resources on such trials would have an adverse effect on our operating results and financial condition. In jurisdictions outside the United States, we or our collaborators must receive marketing authorizations from the appropriate regulatory authorities before commercializing our drugs. Regulatory approval processes outside the United States generally include all of the aforementioned requirements and risks associated with FDA approval. If we or our collaborators are unable to design, conduct and complete successful clinical

trials, our drug candidates will not be able to receive regulatory approval. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive nonclinical testing and clinical trials that the product is both safe and effective for use in each target indication. Results from early clinical trials may not support moving a drug candidate to later- stage clinical trials. Phase 3 clinical trials may not demonstrate the safety or efficacy of our drug candidates. Success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. Results of later clinical trials may not replicate the results of prior clinical trials and preclinical studies. For example, our RELIANCE I study did not achieve its primary endpoint, statistically significant improvements in depression symptoms compared to placebo on Day 28, even though our Phase 2 study was positive. Further, our monotherapy Phase 3 study, RELIANCE III, also did not meet its primary endpoint, statistically significant improvements in depression symptoms compared to placebo on Day 28. Even if our RELIANCE II **, RELIGHT** or other **potential** Phase 3 clinical trials are positive, we or our collaborators may have to commit substantial time and additional resources to conducting further preclinical studies and clinical trials before obtaining FDA approval for any of our drug candidates. ~~Our~~ **Clinical trial results from the study of depression are inherently difficult to predict. In addition, our** clinical trials and our future clinical trials for esmethadone measure clinical symptoms, such as depression that are not biologically measurable. The primary measure of depression is subjective and can be influenced by factors outside of our control, and can vary widely from day to day for a particular patient, and from patient to patient and site to site within a clinical study. The results we have obtained in completed animal studies or we have observed in our clinical trials conducted to date may not be predictive of results from our future clinical trials. For example, our RELIANCE III and RELIANCE I studies did not achieve their primary endpoints, statistically significant improvements in depression symptoms compared to placebo on Day 28 ~~. In addition, clinical trial results from the study of depression are inherently difficult to predict~~ . Clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous requirements. The clinical trial process also consumes a significant amount of time. Furthermore, if participating patients in clinical trials suffer drug- related adverse reactions during the course of such clinical trials, or if we, our collaborators or the FDA believe that participating patients are being exposed to unacceptable health risks, such clinical trials will have to be suspended or terminated. Failure can occur at any stage of the clinical trials, and we or our collaborators could encounter problems that cause abandonment or repetition of clinical trials. We have a limited history of developing drug candidates. We do not know whether any of our ongoing or planned clinical trials will result in marketable drugs. In addition, completion of clinical trials can be delayed by numerous factors, including: ● delays in identifying and agreeing on acceptable terms with prospective clinical trial sites; ● slower than expected rates of patient recruitment and enrollment; ● unanticipated patient dropout rates; and ● increases in time required to complete monitoring of patients during or after participation in a clinical trial. Any of these delays could significantly impact the timing, approval and commercialization of our drug candidates and could significantly increase our overall costs of drug development. We cannot predict whether regulatory agencies will determine that the data from our clinical trials support marketing approval. The FDA' s and other regulatory agencies' ~~decision~~ **decisions** to approve our ~~depression~~ product ~~candidate~~ **candidates** will depend on our ability to demonstrate ~~with substantial clinical evidence~~ through adequate well- controlled clinical trials, that the product candidate is effective **. For esmethadone product candidate** , ~~as~~ **efficacy is** measured statistically by comparing the overall improvement in depression in actively- treated patients against improvement in depression in the control group (a placebo control). However, there is a possibility that our data may fail to show a statistically significant difference from the placebo control or the active control. For example, our RELIANCE III and RELIANCE I studies did not achieve their primary endpoints, statistically significant improvements in depression symptoms compared to placebo on Day 28. Alternatively, there is a possibility that our data may be statistically significant, but that the actual clinical benefit of the product candidates may not be considered to be clinically significant, clinically relevant or clinically meaningful. Even if we believe that the data from our trials will support marketing approval in the United States or in Europe, we cannot predict whether the agencies will agree with our analysis and approve our applications. Developments by competitors may establish standards of care that affect our ability to conduct our clinical trials as planned. Changes in standards related to clinical trial design could affect our ability to design and conduct clinical trials as planned. In that case, both the cost and the amount of time required to conduct a clinical trial could increase ~~. The DEA through its quota system limits the availability of the active ingredients in certain of our current drug candidates and, as a result, the Company' s quotas for these ingredients may not be sufficient to complete clinical trials, or to meet commercial demand or may result in clinical delays. The DEA regulates certain controlled substance chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of abuse and Schedule V substances the lowest risk. Esmethadone is the single isomer of methadone, a Schedule II compound, and its handling (including manufacture, research, shipment, storage, sale and use) is subject to a high degree of federal and state oversight and regulation. Furthermore, the amount of Schedule II substances that can be obtained for clinical trials and commercial distribution is limited by the DEA through its quota system. Quotas may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that federal statutes and DEA regulations concerning applicable quotas may interfere with the supply of the drugs used in clinical trials for our product candidates, and, in the future, the ability to manufacture and distribute esmethadone in the volume needed to meet commercial demand~~ . Conducting clinical trials of our drug candidates or commercial sales of a drug candidate may expose us to expensive product liability claims and we may not be able to maintain product liability insurance on reasonable terms or at all. The risk of product liability is inherent in the testing of pharmaceutical products. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or terminate testing of one or more of our drug candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against product liability claims could prevent or inhibit the commercialization of our drug candidates. We currently carry clinical trial insurance but do not carry product liability insurance. If we successfully commercialize our drug candidates, we may face product liability claims, regardless of FDA approval for commercial manufacturing and sale. We may

not be able to obtain such insurance at a reasonable cost, if at all. Even if our agreements with any current or future corporate collaborators entitle us to indemnification against product liability losses, such indemnification may not be available or adequate should any claim arise. If our drug candidates receive regulatory approval, we and our collaborators will also be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we and our collaborators may also be subject to additional FDA post- marketing obligations or new regulations, all of which may result in significant expense and limit our and our collaborators' ability to commercialize our drugs. Any regulatory approvals that our drug candidates receive may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for costly post- marketing follow- up studies. In addition, if the FDA approves any of our drug candidates, the manufacturing processes, labeling, packaging, distribution, post- approval monitoring and adverse event reporting, storage, import, export, advertising, promotion and record keeping for the drug will be subject to extensive and ongoing regulatory requirements. The FDA has significant post- market authority, including the authority to require labeling changes based on new safety information and to require post- market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The manufacturing facilities used to manufacture our product candidates will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMPs requirements. The discovery of any new or previously unknown problems with our third- party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote our product candidates in a manner inconsistent with FDA- approved labeling or otherwise not in compliance with FDA regulations, we may be subject to enforcement action. If we or our collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the United States or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning or untitled letters, holds on clinical trials, suspension or withdrawal of regulatory approval, product recalls and seizures, administrative detention of products, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution. The FDA' s policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. Fast Track Designation may not lead to a faster development or regulatory review or approval process. We have obtained Fast Track Designation for esmethadone for the adjunctive treatment of MDD. Fast Track Designation is granted if a drug is intended for the treatment of a serious or life- threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition. Fast Track Designation does not guarantee a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Even though we have obtained orphan drug designation in the United States for esmethadone for the treatment of postherpetic neuralgia, we may not obtain or maintain orphan drug exclusivity for that product candidate, and we may not obtain orphan drug designation or exclusivity for any of our other product candidates or indications. The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals in the United States. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the ~~product~~ **active ingredient** is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same ~~drug~~ **active ingredient** for the same disease for seven years. Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. We have obtained orphan drug designation for esmethadone for the treatment of postherpetic neuralgia. If the product candidate were to obtain orphan drug exclusivity upon approval, such exclusivity would prevent the FDA from approving another application to market a drug containing the same active moiety 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. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use, such as MDD, that is broader than the indication for which it received orphan designation. Even though we have received orphan drug designation for esmethadone for the treatment of postherpetic neuralgia, we may not be the first to obtain marketing approval for this active moiety for the orphan- designated indication due to the uncertainties associated with developing pharmaceutical product candidates. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or a drug with the same active moiety can be approved for a different indication. Orphan drug designation by the FDA neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, even if we intend to seek orphan drug designation for other product candidates or indications, we may never receive such designations or obtain orphan drug exclusivity. We may not be able to obtain marketing exclusivity under the Hatch- Waxman Amendments or equivalent regulatory data exclusivity protection in other jurisdictions for our products. We intend to rely, in part, on Hatch-Waxman exclusivity for the commercialization of our products in the United States, if approved. The Hatch- Waxman Amendments provide marketing exclusivity to the first applicant to gain approval of an NDA under specific provisions of the **FDCA** ~~Federal Food, Drug, and Cosmetic Act~~ . For esmethadone, which we intend to elect to have not be considered the same active ingredient as methadone and therefore an NCE, we anticipate obtaining 5- year exclusivity. If FDA were to determine that we do not meet the requirements to make the election, we may not be able to obtain 5- year exclusivity for the product. In

addition, under the statute, this election currently may only be made in an NDA submitted before October 1, 2027. There can be no assurance that European authorities will grant data exclusivity for esmethadone, because it does not contain a new active molecule. Even if European data exclusivity is granted for esmethadone, this may not protect us from direct competition. A competitor (s) with a generic version of our product may be able to obtain approval of its product during our product' s period of data exclusivity, by submitting a marketing authorization application (MAA) with a less than full package of nonclinical and clinical data. We may need to focus our future efforts in new therapeutic areas where we have little or no experience. Although our primary strategic interest is in the areas of depression, esmethadone has potential benefits in other therapeutic areas. If our drug development efforts in depression fail, or if the competitive landscape or investment climate for antidepressant drug development is less attractive, we may need to change the company' s strategic focus to include development of our product candidates, or of newly acquired product candidates, for therapeutic areas other than depression. We have very limited drug development experience in other therapeutic areas and we may be unsuccessful in making this change from a depression company to a company with a focus in areas other than depression **, such as metabolic disorders with psilocybin,** or a company with a focus in multiple therapeutic areas including depression. Our product candidates contain controlled substances, the supply of which may be limited by U. S. statutes and regulations, and the use of which may generate public controversy. The active ingredients in esmethadone **and psilocybin** are listed by the CSA and regulations promulgated by the DEA as controlled substances. The CSA and regulations promulgated by the DEA regulate certain drug substances in Schedule I, II, III, IV or V, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. These product candidates are also subject to the CSA and DEA regulations relating to their handling (i. e., manufacturing, storage, distribution, prescribing and dispensing procedures). **Furthermore, the amount of controlled substances that can be obtained for clinical trials and commercial distribution is limited by the DEA through its quota system. Quotas may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that federal statutes and DEA regulations concerning applicable quotas may interfere with the supply of the drugs used in clinical trials for our product candidates and the ability to manufacture and distribute our product candidates, if approved, in the volume needed to meet commercial demand.** Products containing controlled substances may generate public controversy. Opponents of these products may seek restrictions on marketing and withdrawal of any regulatory approvals. In addition, these opponents may seek to generate negative publicity in an effort to persuade the medical community to reject these products. Political pressures and adverse publicity could lead to delays in, and increased expenses for, and limit or restrict the introduction and marketing of our product candidates. Failure to comply with the CSA or DEA regulations, or the cost of compliance with these regulations, may adversely affect our business. Esmethadone ~~is~~ **and psilocybin are** subject to extensive regulation by the DEA. Although esmethadone is substantially devoid of opioid activity, and psychotomimetic effects, it is currently classified as a Schedule II drug. Upon approval, the DEA may continue to designate it as a controlled substance falling under a DEA controlled substance schedule. Esmethadone is produced by separation from racemic methadone, a scheduled drug subject to extensive regulation by the DEA. **Any psilocybin- containing product candidate we develop is also subject to extensive regulation by the DEA as a Schedule I substance.** The manufacture, shipment, storage, sale and use of controlled substances are highly regulated, including security, recordkeeping and reporting obligations enforced by the DEA. Schedule **I substances by definition have a high potential for abuse, have no currently " accepted medical use " in the United States, lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the United States. Schedule I and** II substances (as well as substances defined as narcotics in any Schedule) are subject to the strictest regulatory requirements and restrictions involving registration, storage, security, recordkeeping and reporting. In particular, distribution and dispensing of Schedule II drugs are strictly controlled. For example, all Schedule II drug prescriptions cannot be refilled and must contain a written or electronic signature of a practitioner when presented to a pharmacy. This high degree of regulation can result in significant costs in order to comply with the required regulations, which may have an adverse effect on the development and commercialization of our product candidates. The DEA limits the availability and production of all scheduled substances, including esmethadone **and psilocybin** , through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. In future years, we may need greater amounts of controlled substances to sustain our development program, and we will need significantly greater amounts to implement our commercialization plans if the FDA approves our proposed formulations. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for scheduled controlled substances or a failure to increase it over time as we anticipate could delay or stop the clinical development or commercial sale of some of our products or product candidates. This could have a material adverse effect on our business, results of operations, financial condition and prospects **. Psilocybin is currently classified as a Schedule I drug in the United States, and any product containing this substance must be rescheduled to be marketed. There can be no assurance that the DEA will make a favorable scheduling decision. Even assuming categorization as a Schedule II or lower controlled substance (i. e., Schedule III, IV or V) at the federal level, such substances would also require scheduling determinations under state laws and regulations. If approved by FDA, and if the finished dosage form of a future psilocybin- containing drug product is listed by the DEA as a Schedule II, III, or IV controlled substance, its manufacture, importation, exportation, domestic distribution, storage, sale, prescribing, and dispensing will continue to be subject to a significant degree of regulation by the DEA. In addition, the final scheduling process may take significantly longer than the 90- day deadline set forth in the CSA, especially if there are objections to such scheduling, thereby delaying the launch of our psilocybin- containing product candidate in the United States. Furthermore, the FDA, DEA or any comparable foreign regulatory authority could require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse or misuse potential, which could increase the cost and / or delay the launch of any future psilocybin- containing product candidates. In addition, product candidates containing controlled substances are**

subject to regulations relating to manufacturing, storage, distribution, prescribing, and dispensing, including: ● State-controlled substances laws. Individual U. S. states have also established controlled substance laws and regulations. Though state- controlled substances laws often mirror federal law, because the states are separate jurisdictions, they will need to separately reschedule any future psilocybin- containing drug products we develop, if approved by FDA. State scheduling may delay commercial sale of any product for which we obtain federal regulatory approval and adverse scheduling would have a material adverse effect on the commercial attractiveness of such product. We or our vendors must also obtain separate state registrations, permits or licenses in order to be able to obtain, handle, and distribute controlled substances for clinical trials or, if approved, commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law. ● Clinical trials. Because we plan to conduct clinical trials of a psilocybin- containing product candidate in the United States prior to approval, each of our research sites must submit a research protocol to the DEA and obtain and maintain a DEA Schedule I researcher registration that will allow those sites to handle and dispense this product candidate and to obtain the product from our importer. If the DEA delays or denies the grant of a researcher registration or approval of the research protocol to one or more research sites, the clinical trial could be significantly delayed, and we could lose clinical trial sites. The importer for the clinical trials must also obtain a Schedule I importer registration and an import permit for each import. We do not currently conduct any manufacturing or repackaging / relabeling of either psilocybin or the psilocybin- containing product candidate in the United States. The potential reclassification of psilocybin in the United States could create additional regulatory burdens on our operations and negatively affect our results of operations. If psilocybin, rather than just a specific FDA- approved formulation, is rescheduled under the CSA as a Schedule II or lower controlled substance (i. e., Schedule III, IV or V), the ability to conduct research on psilocybin would most likely be improved. However, rescheduling psilocybin may materially alter enforcement policies across many federal and state agencies, primarily FDA and DEA. FDA' s responsibilities include regulating the ingredients as well as the marketing and labeling of drugs sold in interstate commerce. Because it is currently illegal under federal law to produce and sell psilocybin, and because there are no federally recognized medical uses, FDA has historically deferred enforcement related to psilocybin to the DEA. If psilocybin were to be rescheduled to a federally controlled, yet legal, substance, FDA would likely play a more active regulatory role. The DEA would continue to be active in regulating manufacturing, distribution and dispensing of such substances. The potential for multi- agency enforcement post- rescheduling, including state agencies, e. g., Boards of Pharmacy, could threaten or have a materially adverse effect on our business. In addition, if the psilocybin- containing product candidate is scheduled as Schedule II, III, IV or V, we would also need to identify wholesale distributors with the appropriate DEA registrations and authority to distribute the psilocybin- containing product candidate. The failure to obtain, or delay in obtaining, or the loss of any of those registrations could result in increased costs to us. If the psilocybin- containing product candidate is classified as a Schedule II drug, participants in our supply chain may have to maintain enhanced security including specially constructed vaults at manufacturing and distribution facilities. This additional security may also discourage some pharmacies from carrying the product . If a supplier of an active pharmaceutical ingredient (API) or a pharmaceutical excipient fails to provide us sufficient quantities, we may not be able to obtain an alternative supply on a timely or acceptable basis. Our **APIs and** pharmaceutical excipients ~~and other APIs~~ are multisource, although not all sources have an active Drug Master File (DMF) with the FDA. A DMF is a submission to the FDA used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of drugs to support drug development and approval. In addition, some of the countries for our multisource APIs may not be same as our drug manufacturing locations. Thus, any disruption in supply from our preferred vendors could result in significant delays with our pharmaceutical development, clinical trials, NDA submission, NDA approval or commercial sale of the finished product due to contract delays, the need to manufacture a new batch of API, out of specification API, the need for import and export permits, and the failure of the newly sourced API to perform to the standards of the previously sourced API. Modifications to our products, if approved, may require new NDA approvals. After a product candidate receives FDA approval, expanded uses or uses in new indications of our products may require additional clinical trials and new regulatory approvals, including additional IND submissions before we can begin clinical development and supplemental NDA approval prior to marketing and sales. If we are required to conduct additional clinical studies, it would require additional expenditures and impact our operating results. Delays in obtaining required future approvals could adversely affect our ability to introduce new or enhanced products in a timely manner, which in turn would harm our future growth. Delays in the commencement or completion of pharmaceutical development, manufacturing or clinical testing could result in increased costs to us and delay our ability to generate revenues. We do not know whether our pharmaceutical development, manufacturing or clinical testing will be on time or be completed on schedule, if at all. For example, we may encounter delays during the manufacture of pilot scale batches including delays with our contract development or manufacturing organization, sourcing satisfactory quantities of APIs, narcotic import and export permits, sourcing of excipients, contract disputes with our third party vendors and manufacturers, or failure of the product to meet specification. Similar delays may occur a during our cGMP manufacture of the product. The commencement and completion of clinical trials can be disrupted for a variety of reasons, including difficulties in: ● recruiting and enrolling patients to participate in a clinical trial; ● obtaining regulatory approval to commence a clinical trial; ● reaching agreement on acceptable terms with prospective clinical research organizations and trial sites; ● obtaining approval of the ~~institutional review board (~~ IRB ~~)~~ at each site selected for participation in our clinical trials; ● manufacturing sufficient quantities of a product candidate; ● investigator fraud, including data fabrication by clinical trial personnel; and ● diversion of controlled substances by clinical trial personnel. A clinical trial may also be suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including: ● failure to conduct the clinical trial in accordance with regulatory requirements or in accordance with our

clinical protocols; ● inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold; ● unforeseen safety issues; or ● inadequate patient enrollment or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes, which could impact the cost, timing or successful completion of a clinical trial. If we experience delays in the commencement or completion of our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also lead to the denial of regulatory approval of a product candidate. Conducting successful clinical studies may require the enrollment of large numbers of patients, and suitable patients may be difficult to identify and recruit. Patient enrollment in clinical trials and completion of patient participation and follow-up depends on many factors, including the size of the patient population; the nature of the trial protocol; the attractiveness of, or the discomforts and risks associated with, the treatments received by enrolled subjects; the availability of appropriate clinical trial investigators; support staff; the number of ongoing clinical trials in the same indication that compete for the same patients; and proximity of patients to clinical sites and ability to comply with the eligibility and exclusion criteria for participation in the clinical trial and patient compliance. For example, patients may be discouraged from enrolling in our clinical trials if the trial protocol requires them to undergo extensive post- treatment procedures or follow- up to assess the safety and effectiveness of our products or if they determine that the treatments received under the trial protocols are not attractive or involve unacceptable risks or discomforts. Patients may also not participate in our clinical trials if they choose to participate in contemporaneous clinical trials of competitive products. Adverse safety outcomes could affect our ability to conduct our clinical trials or obtain approval of our product candidates. Serious injury or death resulting from a failure of one of our drug candidates during current or future clinical trials could result in the FDA **halting or** delaying our clinical trials or denying or delaying clearance or approval of a product. Even though an adverse event may not be the result of the failure of our drug candidate, FDA or an IRB could delay or halt a clinical trial for an indefinite period of time while an adverse event is reviewed, and likely would do so in the event of multiple such events. Any delay or termination of our current or future clinical trials as a result of the risks summarized above, including delays in obtaining or maintaining required approvals from IRBs, delays in patient enrollment, the failure of patients to continue to participate in a clinical trial, and delays or termination of clinical trials as a result of protocol modifications or adverse events during the trials, may cause an increase in costs and delays in the submission of any NDAs to the FDA, delay the approval and commercialization of our products or result in the failure of the clinical trial, which could adversely affect our business, operating results and prospects. Lengthy delays in the completion of clinical trials of our products would adversely affect our business and prospects and could cause us to cease operations. On November 29, 2006, the FDA required a boxed warning to be added to the Prescribing Information **related to cardiac death** for racemic methadone, a parent compound to our esmethadone ~~related to cardiac death~~. Although the decision was based on case reports and not on a controlled clinical trial, as part of the development of esmethadone **,** we ~~are~~ **currently assess (** and have actively assessed **)** the cardiac safety profile of esmethadone in our Phase 3 clinical trials. There is no assurance that the results of our clinical studies will demonstrate an absence of cardiac adverse events with esmethadone. An adverse safety outcome could result in a similar bolded warning on the label of esmethadone or in a decision not to approve esmethadone, either one of which could have serious consequences for our continued operation. **If approved,** ~~Esmethadone~~ **esmethadone and any psilocybin- containing drug product we successfully develop** may require Risk Evaluation and Mitigation Strategies (REMS). Esmethadone **and any psilocybin- containing drug product we successfully develop** , may require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use. We cannot predict the specific REMS to be required as part of the FDA' s approval of any of our products. Depending on the extent of the REMS requirements, our costs to commercialize our products may increase significantly. Furthermore, controlled substances risks that are not adequately addressed through proposed REMS for our product candidates may also prevent or delay their approval for commercialization. Our products will face significant competition in the markets for such products, and if they are unable to compete successfully, our business will suffer. Our products candidates face, and will continue to face, intense competition from large pharmaceutical companies, specialty pharmaceutical and biotechnology companies as well as academic and research institutions. We compete in an industry that is characterized by: (i) rapid technological change, (ii) evolving industry standards, (iii) emerging competition and (iv) new product introductions. Our competitors have existing products and technologies that will compete with our products and technologies and may develop and commercialize additional products and technologies that will compete with our products and technologies. Because several competing companies and institutions have greater financial resources than us, they may be able to: (i) provide broader services and product lines, (ii) make greater investments in research and development, (R & D), and (iii) carry on larger R & D initiatives. Our competitors also have greater development capabilities than we do and have substantially greater experience in undertaking nonclinical and clinical testing of products, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products. They also have greater name recognition and better access to customers than us. Our chief competitors include companies such as Johnson and Johnson, Abbvie, Pfizer, Eli Lilly, ~~Sage Therapeutics, and~~ Axsome Therapeutics **, and Neumora Therapeutics, Inc.** among others. We may be exposed to liability claims associated with the use of hazardous materials and chemicals. Our research and development activities involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require us to incur substantial compliance costs that could materially adversely affect our business and

financial condition. We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits. The testing and marketing of medical products entail an inherent risk of product liability. We may be held liable if serious adverse reactions from the use of our product candidates occur. 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. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with corporate collaborators. We currently do not carry product liability insurance. We, or any corporate collaborators, may not be able to obtain insurance at a reasonable cost, if at all. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate if any claim arises. Risks Related to Our Intellectual Property Our business depends upon securing and protecting critical intellectual property. Our commercial success will depend in part on our obtaining and maintaining patent, trade secret, copyright and trademark protection of our technologies in the United States and other jurisdictions as well as successfully enforcing this intellectual property and defending this intellectual property against third- party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable intellectual property protection, such as patents or trade secrets, cover them. In particular, we place considerable emphasis on obtaining patent and trade secret protection for significant new technologies, products and processes. Furthermore, the degree of future protection of our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Moreover, the degree of future protection of our proprietary rights is uncertain for products that are currently in the early stages of development because we cannot predict which of these products will ultimately reach the commercial market or whether the commercial versions of these products will incorporate proprietary technologies. Our patent position is highly uncertain and involves complex legal and factual questions. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third- party patents. For example, we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents; we or our licensors might not have been the first to file patent applications for these inventions; others may independently develop similar or alternative technologies or duplicate any of our technologies; it is possible that none of our pending patent applications or the pending patent applications of our licensors will result in issued patents; our issued patents and issued patents of our licensors may not provide a basis for commercially viable technologies, or may not provide us with any competitive advantages, or may be challenged and invalidated by third parties; and, we may not develop additional proprietary technologies that are patentable. As a result, our owned and licensed patents may not be valid and we may not be able to obtain and enforce patents and to maintain trade secret protection for the full commercial extent of our technology. The extent to which we are unable to do so could materially harm our business. Unpatented trade secrets, improvements, confidential know- how and continuing technological innovation are important to our scientific and commercial success. Although we attempt to and will continue to attempt to protect our proprietary information through reliance on trade secret laws and the use of confidentiality agreements with our corporate partners, collaborators, employees and consultants and other appropriate means, these measures may not effectively prevent disclosure of our proprietary information, and, in any event, others may develop independently, or obtain access to, the same or similar information. Certain of our patent rights are licensed to us by third parties. If we fail to comply with the terms of these license agreements, our rights to those patents may be terminated, and we will be unable to conduct our business. If we are found to be infringing on patents or trade secrets owned by others, we may be forced to cease or alter our product development efforts, obtain a license to continue the development or sale of our products, and / or pay damages. Our manufacturing processes and potential products may violate proprietary rights of patents that have been or may be granted to competitors, universities or others, or the trade secrets of those persons and entities. As the pharmaceutical industry expands and more patents are issued, the risk increases that our processes and potential products may give rise to claims that they infringe the patents or trade secrets of others. These other persons could bring legal actions against us claiming damages and seeking to enjoin clinical testing, manufacturing and marketing of the affected product or process. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license in order to continue to conduct clinical tests, manufacture or market the affected product or use the affected process. Required licenses may not be available on acceptable terms, if at all, and the results of litigation are uncertain. If we become involved in litigation or other proceedings, it could consume a substantial portion of our financial resources and the efforts of our personnel. Our ability to protect and enforce our patents does not ~~guaranty~~ **guarantee** that we will secure the right to commercialize our patents. A patent is a limited monopoly right conferred upon an inventor, and his successors in title, in return for the making and disclosing of a new and non-obvious invention. This monopoly is of limited duration but, while in force, allows the patent holder to prevent others from making and / or using his invention. While a patent gives the holder this right to exclude others, it is not a license to commercialize the invention, where other permissions may be required for permissible commercialization to occur. For example, a drug cannot be marketed without the appropriate authorization from the FDA, regardless of the existence of a patent covering the product. Further, the invention, even if patented itself, cannot be commercialized if it infringes the valid patent rights of another party. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative: ● others may be able to make a product that is similar to our current and future product candidates we intend to commercialize that is not covered by the patents that we own or license and have the right to enforce; ● others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; ● it is possible that our current and future patent applications will not lead to issued patents; ● issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result

of legal challenges; and ● our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and we may not develop additional proprietary technologies that are patentable. Risks Related to Government Regulation We may undertake international operations, which will subject us to risks inherent with operations outside of the United States. Although we do not have any foreign operations at this time, we intend to seek to obtain market clearances in foreign markets that we deem to generate significant opportunities. However, even with the cooperation of a commercialization partner, conducting drug development in foreign countries involves inherent risks, including, but not limited to: difficulties in staffing, funding and managing foreign operations; unexpected changes in regulatory requirements; export restrictions; tariffs and other trade barriers; difficulties in protecting, acquiring, enforcing and litigating intellectual property rights; fluctuations in currency exchange rates; and potentially adverse tax consequences. If we were to experience any of the difficulties listed above, or any other difficulties, any international development activities and our overall financial condition may suffer and cause us to reduce or discontinue our international development and registration efforts. We depend on our information technology systems and those of our third- party collaborators, service providers, contractors or consultants. Our internal computer systems, or those of our third- party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, disruptions, or incidents, which could result in a material disruption of our development programs or loss of data or compromise the privacy, security, integrity or confidentiality of sensitive information related to our business and have a material adverse effect on our reputation, business, financial condition or results of operations. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. Our internal technology systems and infrastructure, and those of our current or future third- party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, natural disasters, terrorism, war and telecommunication and electrical failures, denial- of- service attacks, cyber- attacks or cyber- intrusions over the internet, hacking, phishing and other social engineering attacks, persons inside our organizations (including employees or contractors), loss or theft, or persons with access to systems inside our organization. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized foreign governments, groups and individuals with a wide range of motives and expertise. In addition to extracting or accessing sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial- of- service attacks, social engineering and other means to affect service reliability and threaten the security, confidentiality, integrity and availability of information. The prevalent use of mobile devices that access sensitive information also increases the risk of data security incidents which could lead to the loss of confidential information or other intellectual property. While to our knowledge we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third- party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. Failure to comply with existing or future laws and regulations related to privacy or data security could lead to government enforcement actions (which could include civil or criminal fines or penalties), private litigation, other liabilities, and / or adverse publicity. Compliance or the failure to comply with such laws could increase the costs of our products and services, could limit their use or adoption, and could otherwise negatively affect our operating results and business. Regulation of data processing is evolving, as federal, state, and foreign governments continue to adopt new, or modify existing, laws and regulations addressing data privacy and security, and the collection, processing, storage, transfer, and use of data. We and our partners may be subject to current, new, or modified federal, state, and foreign data privacy and protection laws and regulations (e. g., laws and regulations that address data privacy and data security including, without limitation, health data). These new or proposed laws and regulations are subject to differing interpretations and may be inconsistent among jurisdictions, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data. These and other requirements could require us or our partners to incur additional costs to achieve compliance, limit our competitiveness, necessitate the acceptance of more onerous obligations in our contracts, restrict our ability to use, store, transfer, and process data, impact our or our partners' ability to process or use data in order to support the provision of our products or services, affect our or our partners' ability to offer our products and services in certain locations, or cause regulators to reject, limit or disrupt our clinical trial activities. Failure to comply with U. S. and international data privacy and protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties, fines or sanctions), private litigation, and / or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations related to security or privacy, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business. Compliance with data protection laws may be time- consuming, require additional resources and could result in increased expenses, reduce overall demand for our products and services and make it more difficult to meet expectations of or commitments to customers or partners. Our operations and relationships with future customers, providers 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 penalties including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. Healthcare providers and third- party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with providers, third- party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we obtain marketing approval. Restrictions under applicable U. S. federal and state healthcare laws and regulations include the following: ● the federal Anti- Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti- Kickback Statute or specific intent to violate it in order to have committed a violation; ● federal false claims laws, including the federal False Claims Act, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the U. S. federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act; ● HIPAA **, as amended by HITECH,** imposes criminal and civil liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; ● the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children' s Health Insurance Program, with specific exceptions, to report payments and other transfers of value provided during the previous year to physicians, as defined by such law, physician assistants, certain types of advance practice nurses, and teaching hospitals, as well as certain ownership and investment interests held by such physicians and their immediate family, which includes annual data collection and reporting obligations; **and** ● analogous state and foreign laws and regulations, such as state anti- kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third- party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures **or** ~~; and ● some state laws require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require~~ drug **pricing** ~~manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures~~ . Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of product candidates from government- funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs. Enacted and future legislation may affect the prices we may set. The full effect of recent United States healthcare reform and other changes in the healthcare industry, laws, and regulations and in healthcare spending is currently unknown, and the reform and other changes may adversely affect our business model. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, affect our ability to profitably sell any products for which we obtain marketing approval. The commercial potential for our products, if any, could also be affected by changes in healthcare spending and policy in the United States and abroad. New laws, regulations, or judicial decisions or new interpretations of existing laws, regulations, or decisions, related to healthcare availability, the method of delivery, or payment for healthcare products and services could adversely affect our business, operations, and financial condition, if and when we are able to obtain marketing approval and commercialize our products. For example, the ACA was enacted in 2010 with a goal, among others, of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The ACA, among other things, expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program, imposed a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products, and enacted substantial provisions affecting compliance, which may affect our business practices with healthcare practitioners. There have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs in general and the cost of pharmaceuticals in particular. These initiatives recently culminated in the enactment of the ~~Inflation Reduction Act, or~~ IRA ~~,~~ in August 2022, which, among other things, ~~will allow~~ **allows** HHS to **directly** negotiate the selling price of ~~certain~~ **a statutorily speficied number of** drugs and biologics **each year** that CMS reimburses under Medicare Part B and Part D **.** ~~(excluding drugs and biologies that are designated and approved for only~~ **Only** ~~one rare disease or~~

~~condition), although only~~ high- expenditure single- source biologics that have been approved for at least 11 years (7 years for **single- source** drugs) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. ~~The~~ **Negotiations for Medicare Part D products begin in 2024 with the** negotiated **price taking effect in 2026, and negotiations for Medicare Part B products begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations. HHS will announce the negotiated maximum fair** prices **by September 1, 2024, and this price cap** , which **cannot exceed** ~~will first become effective in 2026, will be capped at~~ a statutory ceiling price ~~representing a significant discount~~ **, will come into effect on January 1, 2026. A drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded** from ~~average~~ **the IRA' s** ~~prices~~ - **price** ~~to wholesalers and direct purchasers. Beginning in October 2022~~ **negotiation requirements, but will lose that exclusion if it has designations for more than one rare disease** ~~for~~ - **or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The IRA also imposes rebates on** Medicare Part D and ~~January 2023 for Medicare Part B, the law also penalizes drug manufacturers that increase prices of Medicare Part D and~~ Part B drugs **whose prices have increased** at a rate greater than the rate of inflation. In addition, the law eliminates **, beginning in 2025,** the **coverage gap** ~~" donut hole "~~ under Medicare Part D ~~beginning in 2025~~ by significantly lowering the beneficiary maximum out- of- pocket cost **and requiring manufacturers to subsidize,** through a newly established manufacturer discount program **, 10 % of Part D enrollees' prescriptions costs for brand drugs below the out- of- pocket maximum, and 20 % once the out- of- pocket maximum has been reached** . The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. **For example, the provisions related to the negotiation of selling prices of high- expenditure single- source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers.** Thus, **while it is unclear how** the IRA **will implemented, it** will likely have a significant impact on the pharmaceutical industry. Further, at the U. S. state level, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discount requirements, marketing cost disclosure **, price gouging prohibitions,** and price transparency reporting. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services or otherwise negatively impact our business model. Risks Related to Our Reliance on Third Parties We have no manufacturing capabilities and depend on other parties for our manufacturing operations. If these manufacturers fail to meet our requirements and strict regulatory requirements, our product development and commercialization efforts may be materially harmed. We do not own or operate facilities for drug manufacturing, storage, distribution or quality testing. We currently rely, and may continue to rely, on third- party contract manufacturers to manufacture APIs, drug products and other components of our product candidates. Reliance on third- party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. We, and our suppliers and manufacturers, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA and foreign regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of our product candidates. Moreover, we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements. In the event that any of our manufacturers fail to comply with such requirements or to perform their obligations in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to enter into an agreement with other third parties, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to original manufacturers and we may have difficulty transferring such to other third parties. These factors would increase our reliance on such manufacturers or require us to obtain a license from such manufacturers in order to enable us, or to have other third parties, manufacture our product candidates. We expect to continue to rely on third- party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce our products will be subject to periodic review and inspection by the FDA and foreign regulatory authorities, including for continued compliance with cGMP requirements, quality control, quality assurance and corresponding maintenance of records and documents. If we are unable to obtain or maintain third- party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Or a third parties' failure to execute on our manufacturing requirements, comply with cGMPs or maintain a compliance status acceptable to the FDA or foreign regulatory authorities could adversely affect our business in a number of ways, including: ● an inability to initiate or continue clinical trials of product candidates under development; ● delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates; ● loss of the cooperation of existing or future collaborators; ● subjecting third- party manufacturing

facilities to additional inspections by regulatory authorities; ● requirements to cease distribution or to recall batches of our product candidates; and ● in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products. Our contract manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our contract manufacturers were to encounter difficulties, our ability to provide our product candidates to patients in preclinical and clinical trials, or to provide product for treatment of patients once approved, would be jeopardized. We intend to rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not perform as contractually required or otherwise expected, we may not be able to obtain regulatory approval for our product candidates. We do not currently conduct preclinical studies or clinical trials on our own, and instead will rely on third parties, such as contract research organizations (CROs), medical institutions, clinical investigators and contract laboratories, to assist us with our preclinical studies and clinical trials. Accordingly, we have less control over the timing, quality and other aspects of preclinical studies and clinical trials than if we conducted them on our own. These investigators, CROs and consultants are not our employees and we will have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we may contract might not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful. If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we will be responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial as well as applicable legal and regulatory requirements. The FDA generally requires preclinical studies to be conducted in accordance with good laboratory practices and clinical trials to be conducted in accordance with good clinical practices, including for designing, conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control will not relieve us of these responsibilities and requirements. Any adverse development or delay in our preclinical studies or clinical trials as a result of our reliance on third parties could have a material and adverse effect on our business, financial condition, results of operations and prospects. Risks Related to Ownership of Our Common Stock There is a limited market for our common stock that may make it more difficult to dispose of your stock. Our common stock is currently listed on the Nasdaq Global Select Market under the symbol " RLMD ". There is a limited trading market for our common stock. Accordingly, there can be no assurance as to the liquidity of any markets that may develop for our common stock, the ability of holders of our common stock to sell shares of our common stock, or the prices at which holders may be able to sell their common stock. A sale of a substantial number of shares of our common stock may cause the price of the common stock to decline. If our stockholders sell substantial amounts of our common stock in the public market, the market price of our common stock could fall. These sales also may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate. Stockholders who have held their shares for at least six months are able to sell their shares pursuant to Rule 144 under the Securities Act of 1933, as amended (the Securities Act). We have registered under separate registration statements in aggregate up to 21, 041, 717 shares of our common stock for sale into the public market by certain selling stockholders named therein. These shares represent a large number of shares of our common stock, and if sold in the market all at once or at about the same time, could depress the market price of our common stock during the period the registration statement remains effective and could also affect our ability to raise equity capital. We are subject to the reporting requirements of federal securities laws, which can be expensive and may divert resources from other projects, thus impairing our ability grow. We are a public reporting company and, accordingly, subject to the information and reporting requirements of the Exchange Act and other federal securities laws, including compliance with the Sarbanes- Oxley Act of 2002 (the Sarbanes- Oxley Act). The costs of preparing and filing annual and quarterly reports, proxy statements and other information with the SEC and furnishing audited reports to stockholders cause our expenses to be higher than they would be if we remained privately held. It may be time - consuming, difficult and costly for us to develop and implement the internal controls and reporting procedures required by the Sarbanes- Oxley Act. We may need to hire additional financial reporting, internal controls and other finance personnel in order to develop and implement appropriate internal controls and reporting procedures. If we are unable to comply with the internal controls requirements of the Sarbanes- Oxley Act, then we may not be able to obtain the independent accountant certifications required by such act, which may preclude us from keeping our filings with the SEC current. If we fail to establish and maintain an effective system of internal control, we may not be able to report our financial results accurately or to prevent fraud. Any inability to report and file our financial results accurately and timely could harm our reputation and adversely impact the trading price of our common stock. Effective internal control is necessary for us to provide reliable financial reports and prevent fraud. If we cannot provide reliable financial reports or prevent fraud, we may not be able to manage our business as effectively as we would if an effective control environment existed, and our business and reputation with investors may be harmed. As a result, our small size and any undiscovered current internal control deficiencies may adversely affect our financial condition, results of operation and access to capital. We have not performed an in- depth analysis to determine if historical un- discovered failures of internal controls exist , and may in the future discover areas of our internal control that need improvement. In addition, as a smaller reporting company, our independent registered public accounting firm is not required to formally attest to the effectiveness of our internal control over financial reporting so long as we remain a smaller reporting company, which could increase the likelihood of undiscovered errors in our internal controls or reported financial statements as compared to issuers whose independent registered public accounting firms have provided such attestations. Our stock price may be volatile. The market price of our common stock is likely to be highly

volatile and could fluctuate widely in price in response to various factors, many of which are beyond our control, including the following: ● changes in our industry; ● competitive pricing pressures; ● our ability to obtain working capital financing; ● additions or departures of key personnel; ● limited " public float " in the hands of a small number of persons whose sales or lack of sales could result in positive or negative pricing pressure on the market price for our common stock; ● sales of our common stock; ● our ability to execute our business plan; ● operating results that fall below expectations; ● negative or poor clinical results; ● regulatory developments; ● economic and other external factors; ● period- to- period fluctuations in our financial results; and ● inability to develop or acquire new or needed technology or products. In addition, the securities markets have from time - to - time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. These market fluctuations may also materially and adversely affect the market price of our common stock. The Nevada Revised Statutes and our articles of incorporation and bylaws contain provisions that could discourage, delay or prevent a change in control of our Company, prevent attempts to replace or remove current management and reduce the market price of our stock. Provisions in our articles of incorporation and bylaws may discourage, delay or prevent a merger or acquisition involving us that our stockholders may consider favorable. For example, our articles of incorporation authorize our board of directors to issue up to 200, 000, 000 shares of " blank check " preferred stock. As a result, without further stockholder approval, the board of directors has the authority to attach special rights, including voting and dividend rights, to this preferred stock. With these rights, preferred stockholders could make it more difficult for a third party to acquire us. We are also subject to the anti- takeover provisions of the Nevada Revised Statutes (NRS). Depending on the number of residents in the state of Nevada who own our shares, we could be subject to the provisions of Sections 78. 378 et seq. of the Nevada Revised Statutes, which, unless otherwise provided in the Company' s articles of incorporation or by- laws, restricts the ability of an acquiring person to obtain a controlling interest of 20 % or more of our voting shares. Our articles of incorporation and by- laws do not contain any provision which would currently keep the change of control restrictions of Section 78. 378 from applying to us. In addition, our articles of incorporation and amended and restated bylaws provide that our board of directors is classified into three classes of directors with staggered three- year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three- year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time - consuming for stockholders to replace a majority of the directors on a classified board of directors. Our bylaws provides that a Nevada court and the federal district courts of the United States will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Pursuant to our bylaws, to the fullest extent permitted by law, and unless we consent in writing to the selection of an alternative forum, the Eighth Judicial District Court of Clark County, Nevada, is the sole and exclusive forum for any stockholder (including a beneficial owner of stock) to bring (a) any derivative action or proceeding brought in the name or right of the Company or on our behalf, (b) any action asserting a claim of, or a claim based on, breach of any fiduciary duty owed by any current or former director, officer, employee, agent or stockholder of the Company to the Company or the Company' s stockholders, (c) any action arising or asserting a claim arising pursuant to any provision of NRS Chapters 78 or 92A or any provision of the articles of incorporation or our bylaws or (d) any action asserting a claim against us or any current or former director, officer, employee or stockholder (including a beneficial owner of stock) governed by the internal affairs doctrine, including, without limitation, any action to interpret, apply, enforce or determine the validity of our articles of incorporation or bylaws. By its terms, to the fullest extent permitted by law, our forum selection provision applies to actions arising under the Securities Act or Exchange Act. (However, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder, and the Company does not intend for its exclusive forum jurisdiction provision to apply to Exchange Act claims.) These choice of forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees. If a court were to find the choice of forum provision contained in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business.