Risk Factors Comparison 2025-03-14 to 2024-03-28 Form: 10-K

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Risks Related to Our Financial Position and Need for Additional Capital • We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future. We have never been **,** and may never be **,** profitable. • We will require substantial additional capital **to finance our operations** . If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and / or eliminate one or more of our research and drug development programs, future commercialization efforts or other operations. • Our auditors have expressed substantial doubt about our ability to continue as a going concern, and we may not be able to continue as a going concern if we do not obtain additional financing. Risks Related to Research and Development and the Pharmaceutical Industry • Our business is highly dependent on the success of our lead product candidate, GRI- 0621, and any other product candidates that we may advance into clinical development. All of our product candidates will require significant additional development before we may be able to seek regulatory approval and launch a product commercially. • Clinical development involves a lengthy, complex, and expensive process, with an uncertain outcome. In addition, the results of preclinical studies and early- stage clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. Risks Related to Commercialization of Our Product Candidates • Failure to obtain or maintain adequate reimbursement or insurance coverage for our approved product candidates, if any, could limit our ability to market those product candidates and decrease our ability to generate revenue. • Even if we obtain U. S. Food and Drug Administration (FDA) approval of any of our product candidates **, if any** , we may never obtain approval or commercialize these product candidates outside of the United States, which could limit our ability to realize their full market potential. • We currently have no marketing and sales organization and have no experience as a company in commercializing products. We would have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue from any of our product candidates that may be approved. • Our relationships with healthcare providers, physicians, prescribers, purchasers, third- party payors, charitable organizations and patients will be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. • Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations. • Inadequate funding for the FDA, the SEC and / or other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. • If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business, financial condition or results of operations. Risks Related to Our Intellectual Property • Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection. • We may enter into license or other collaboration agreements in the future that may impose certain obligations on us. If we fail to comply with our obligations under such future agreements with third parties, we could lose license rights that may be important to our future business. • Third- party claims of intellectual property infringement may be costly and time consuming to defend, and could prevent or delay our product discovery, development and commercialization efforts. Risks Related to Our Reliance on Third Parties • We rely on third parties to conduct our clinical trials, manufacture our product candidates and perform other services. If these third parties do not successfully carry out their contractual duties, meet expected timelines or otherwise conduct the trials as required or perform and comply with regulatory **or contractual** requirements, we may not be able to successfully complete clinical development, obtain regulatory approval or commercialize our product candidates when expected or at all, and our business could be substantially harmed. • Because we rely on third- party manufacturing and supply vendors, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality. • We may in the future seek to enter into collaborations with third parties for the development and commercialization of our product candidates, and our future collaborations will be important to our business. If we are unable to enter into collaborations, or if these collaborations are not successful, our business could be adversely affected. Risks Related to Managing Our Business and Operations • If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to develop current product candidates or identify and develop new product candidates will be impaired, could result in loss of markets or market share and could make us less competitive. • We may be unable to adequately protect our **internal** information systems **, or those used by our CROs, clinical sites, or other contractors or consultants upon which we rely,** from cyberattacks **, compromises, cybersecurity incidents, or other disruptions** , which could result in the ~~disclosure~~ **compromise** of ~~confidential~~ **sensitive** or proprietary information, ~~including personal data~~ **lead to operational or service interruption** , ~~damage~~ **harm** our reputation, and subject us to **litigation, fines and other** significant financial and legal exposure **, and other material and adverse consequences** . Risks Related to Financing, our Common Stock ~~,~~ and Capital Requirements • We expect the stock price of our Common Stock to be highly volatile. • Future sales and issuances of our securities could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall. • The **February** ~~listing of shares of our Common Stock does not currently comply with the rules of The Nasdaq Capital Market or any other Nasdaq Market tier. A delisting of our Common Stock from Nasdaq could subject us to substantial financial penalties and / or~~

~~adversely affect our ability to raise additional capital through the public or private sale of equity securities and our investors' ability to dispose of, or obtain accurate quotations as to the market value of, our Common Stock. • The January 2024~~ **2025** Reverse Stock Split may have caused our stock price to decline relative to its value before the split and ~~decreased~~ **likely has reduced** the liquidity of shares of our Common Stock. MARKET, INDUSTRY AND OTHER DATA This Annual Report contains estimates, projections and other information concerning our industry, our business and the markets for our drug candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market and similar data set forth in this Annual Report from our internal estimates and research and from independent industry publications, governmental publications, reports by market research firms or other independent sources that we believe to be reliable sources. In some cases, we do not expressly refer to the sources from which this data is derived. Industry publications and third- party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the industry in which we operate, and our management' s understanding of industry conditions. While we believe our internal research is reliable, it has not been verified by an independent source. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. We are responsible for all of the disclosure contained in this Annual Report, and we believe these industry publications and third- party research, surveys and studies are reliable. While we are not aware of any misstatements regarding any third- party information presented in this Annual Report, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section entitled " **Item 1A.** Risk Factors " in this Annual Report, and elsewhere in this Annual Report. PART I Item 1. BUSINESS **.** Overview We are a clinical- stage biopharmaceutical company focused on discovering, developing, and commercializing innovative therapies that target serious diseases associated with dysregulated immune responses leading to inflammatory, fibrotic, and autoimmune disorders. Our goal is to be an industry leader in developing therapies to treat these diseases and to improve the lives of patients suffering from such diseases. Our lead product candidate, GRI- 0621, is an oral inhibitor of type 1 **invariant** Natural Killer T **(iNKT)** cells. GRI- 0621 is also an oral formulation of tazarotene, a synthetic RAR- beta and gamma selective agonist, that is approved in the United States for topical treatment of psoriasis and acne. As of December 31, ~~2023~~ **2024** , it has been evaluated in over 1, 700 patients as an oral product for up to 52- weeks. We are developing GRI- 0621 for the treatment of severe fibrotic lung diseases such as idiopathic pulmonary fibrosis (IPF), a life- threatening progressive fibrotic disease of the lung that affects approximately 140, 000 people in the United States, with up to 40, 000 new cases per year in the United States. Some estimate that IPF affects 3 million people globally. While there are currently two approved therapies for the treatment of lung fibrosis, neither has been associated with improvements in overall survival, and both therapies have been associated with significant side effects leading to poor therapeutic adherence. In preliminary data from our trials to date with GRI- 0621, and earlier trials with oral tazarotene, we have observed GRI- 0621 to be well- tolerated and to inhibit iNKT cell activity in subjects. We and others have shown that activated iNKT are upregulated in IPF, primary sclerosing cholangitis (PSC), non- alcoholic steatohepatitis (NASH), alcoholic liver disease (ALD), systemic lupus erythematosus disease (SLE), multiple sclerosis (MS), ulcerative colitis (UC) patients, as well as other indications. In these patients activated iNKT cells are correlated with more severe disease. The U. S. Food and Drug Administration (FDA) has cleared our IND application for GRI- 0621 for the treatment of IPF and we plan to evaluate GRI- 0621 in a randomized, double- blind, multi- center Phase 2a biomarker study, for which we commenced enrollment in December 2023. ~~We~~ **Based on our current projections, we** expect topline results from this trial to be available in the ~~second half~~ **third quarter** of **2025. Additionally, on March 1,** 2024 **, we received authorization of our clinical trial application (CTA) from the United Kingdom Medicines and Healthcare Products Regulatory Agency (MHRA) to initiate the Phase 2a biomarker study evaluating GRI- 0621 for the treatment of IPF in the United Kingdom. On September 24, 2024, we received approval from the Australian Human Research Ethics Committee (HREC) to initiate the Phase2a biomarker study evaluating GRI- 0621 for the treatment of IPF in Australia, after previously receiving authorization on our CTA from the Australian MHRA** . Our product candidate portfolio also includes GRI- 0803 and a proprietary library of 500 compounds. GRI- 0803, the lead molecule selected from the library, is a novel oral agonist of type 2 **diverse** Natural Killer T (~~type 2 NKT~~ **dNKT**) cells. We are developing GRI- 0803 for the treatment of autoimmune disorders, with much of our preclinical work in SLE or lupus and MS. In lupus, the immune system mistakenly attacks its own healthy tissues, especially joints and skin, but can affect almost every organ and tissue of the body. The condition can be fatal, and often causes debilitating bouts of fatigue and pain that prevent nearly half of adult patients from working. Lupus affects between 160, 000- 200, 000 patients in the United States, with around 80, 000 – 100, 000 patients in the United States suffering from kidney nephritis, one of the most serious manifestations of SLE, typically within five years of diagnosis. There is no cure for lupus, but medical interventions and lifestyle changes can help control it. SLE treatment consists primarily of immunosuppressive drugs that inhibit the activity of the immune system. Only two drugs have been approved for lupus in the past 50 years, and new treatment options are sorely needed. Subject to IND clearance, we intend to evaluate GRI- 0803 in a Phase 1a and 1b trial initially targeting SLE. We expect to file an IND with respect to this Phase 1a and 1b trial in ~~the first half of 2024~~ **2025** . We will continue to evaluate indications to select the best fit for further development of the program, but our initial focus is on lupus. Our Pipeline We have retained global development and commercialization rights to all of the product candidates in our pipeline. The chart below summarizes key information about our programs. We are also progressing several preclinical and clinical assets that have shown promise in ~~pre- clinical~~ **preclinical** models associated with disease. _____ Figure 1. GRI' s pipeline- GRI- 0621 and GRI- 0803 Our initial focus is developing GRI- 0621 for the treatment of IPF. GRI- 0621 is an oral formulation of tazarotene, a synthetic retinoid acid receptor (RAR)- beta and gamma selective agonist that is approved in the United States for

topical treatment of psoriasis and acne. GRI- 0621 inhibits the activity of iNKT cells that have been shown to accumulate in IPF patients and other interstitial lung disease patients. We, and others, have shown that activated iNKT cells are overexpressed in IPF, hepatic and other fibrotic conditions and are significantly correlated with advanced disease. We believe GRI- 0621 has the potential to treat multiple fibrotic and related diseases, including other pulmonary fibrotic diseases, NASH, ALD, renal fibrosis, acute- on- chronic liver failure, drug- induced liver injury (DILI) and other acute indications. In numerous preclinical studies, inhibiting the activity of iNKT cells significantly reduced inflammation, activation of macrophage populations, transforming growth factor (TGF)- beta and fibrosis. There are currently no therapeutics approved that specifically target iNKT cells. We evaluated GRI- 0621 in a pilot Phase 2a trial in 14 hepatically impaired chronic liver disease patients. The study was originally intended to evaluate 60 patients, but we made the administrative decision to halt the study after enrolling 14 patients due to recruitment challenges and updated guidance from the FDA regarding the design of NASH clinical studies. In this limited number of patients, GRI- 0621 was observed to be well **-** tolerated, however, the study was underpowered to meet its endpoints with statistical significance. In December 2023, we commenced enrollment in our Phase 2a trial **in IPF patients** and we expect topline results from this trial to be available in the ~~second half~~ **third quarter** of ~~2024~~ **2025**. We are also developing GRI- 0803, a novel orally administered activator of ~~type 2 NKT~~ **dNKT** cells, from which we observed therapeutic benefit in multiple models of autoimmunity. We believe GRI- 0803 has the potential to treat SLE and related kidney nephritis, MS, autoimmune hepatitis, and other autoimmune disorders. In addition, we have a library of over 500 novel compounds acquired from JADO Technologies GmbH. The library was designed to mimic the structure and function of GRI- 0124 (miltefosine), a potent activator of ~~type 2 NKT~~ **dNKT** cells. GRI- 0803 is the lead product candidate selected from the library. We are built upon decades of experience studying the activity of Natural ~~Killer~~ **Killer** T (NKT) cells and their role in health and disease. Our company was founded by three immunologists, including an internationally recognized leader in NKT cell research who contributed to the initial characterization of NKT subsets, characterized the T cell receptor binding of ~~type 1 and type 2 NKT~~ **iNKT and dNKT** cells with their respective ligands and identified and characterized the role of ~~type 1 and type 2 NKT~~ **iNKT and dNKT** cells in inflammatory, fibrotic, and autoimmune disorders. We believe that our founders' and management' s experience provide unique insights into the activity of NKT cells and their role in chronic inflammatory, fibrotic, and autoimmune disorders. We are led by W. Marc Hertz, Ph. D., our President and Chief Executive Officer, a biotechnology executive who previously served as Chief Executive Officer of Pharmexa, Inc. and Multimeric Biotherapeutics, Inc. and as part of the senior management of Pharmexa A / S. Albert Agro, Ph. D., our Chief Medical Officer, has extensive experience in the ~~biotech~~ **biotechnology** and pharmaceutical industries and previously held senior positions in global clinical development Boehringer Ingelheim International GmbH and Bayer Inc., as well as executive positions at Cynapsus Therapeutics Inc. (Chief Medical Officer), vTv Therapeutics Inc. (Sr. Vice President Development) and Sublimity Therapeutics Limited (Chief Executive Officer). Dr. Agro maintains a faculty appointment at McMaster University in the Department of Pathology and Molecular Medicine. Vipin Kumar Chaturvedi, Ph. D., our Chief Scientific Officer, is an internationally recognized leader in NKT cell research. GRI' s technologies are based on his work identifying NKT cell subsets and their differential roles in inflammatory, fibrotic, and autoimmune disease. Dr. Kumar is ~~a~~ **an Adjunct** Professor **at the University of California, San Diego, and former Professor** of Medicine ~~and heads~~ **where he headed** the Laboratory of Immune Regulation ~~at the University of California, San Diego~~. We are supported by our board of directors (the Board) and clinical advisory boards and have been funded to date by family offices and leading life sciences investors ~~including TEP Biotech, LLC (TEP), Acquipharma Holdings Ltd and Altium Healthcare Inc~~. Our Strategy Our goal is to become a leader in developing and commercializing therapeutics that target diseases with significant unmet needs. Our initial focus is on developing product candidates that target the activity of NKT cells and their role in driving dysregulated immune responses. Our strategy is focused on the following key components: • Efficiently advance the clinical development of GRI- 0621 in IPF. We intend to conduct a randomized double- blind placebo- controlled Phase 2a trial in approximately 36 patients with IPF with topline data expected in the ~~second half~~ **third quarter** of ~~2024~~ **2025**. This orphan disease is therapeutically underserved, and we believe that GRI- 0621 may have the ability to become the first true disease- modifying therapy for these patients. Assuming a positive result in this trial, we plan to initiate a Phase 2b trial that could support an application for conditional approval of GRI- 0621 in the European Union (**the** EU) and could have the potential to be regarded as a registrational trial in the United States. • Advance GRI- 0803 through Phase 1a / 1b studies initially targeting SLE. Subject to IND clearance, we intend to evaluate GRI- 0803 in a Phase 1a and 1b trial initially targeting SLE. We expect to file an IND with respect to this trial in ~~the first half of 2024~~ **2025**. • Leverage our understanding of iNKT and ~~type 2 NKT~~ **dNKT** cells in disease and continue evaluating GRI- 0621, GRI- 0803, and additional product candidates in subsequent indications. We intend to expand our leadership as a company dedicated to developing therapies that directly target the biological processes driving dysregulated immune responses. We also intend to selectively pursue business development opportunities to expand our product portfolio and supporting technologies. • Continue to build a patient- focused company across a broad range of inflammatory, fibrotic and autoimmune diseases. In building a patient- focused company to address the needs of patients, we will work with clinicians, patient advocacy groups, medical centers of excellence, and medical key opinion leaders to better understand the symptoms and consequences of these diseases, to expeditiously develop and provide better treatments to patients, and to increase awareness of these diseases. • Maximize the commercial value of our product candidates. We have retained worldwide development and commercial rights for all our product candidates. We intend to commercialize any products in our portfolio for which we receive regulatory approvals in certain rare indications in the United States and the EU with a limited and targeted commercial team. We also intend to retain the flexibility to evaluate strategic collaborations and to seek partners to commercialize our products in other geographies and for our products in highly prevalent indications which require significant investment to build a commercial infrastructure. NKT Cells and the Immune System Our approach is founded on the discovery that NKT cells are a functional link between the innate and adaptive immune systems and that dysregulated immune responses can be reset by regulating the activity of NKT cells to potentially treat a broad array of acute and chronic

conditions. Figure 2. NKT cells are innate- like T cells that bridge the adaptive and innate immune systems. NKT cells are innate- like T cells that bridge the adaptive and innate immune systems (see Figure 2). They share properties of both NK and T cells, control the expression of key cytokines / chemokines, and are critical regulators of immune responses. iNKT cells are effector T cells that can play a pathogenic role in lung, liver, and autoimmune indications; while ~~type 2 NKT~~ **dNKT** cells are regulatory T cells that inhibit the activity of iNKT cells, as well as other cell types, and support an anti- inflammatory response. ~~Type 2 NKT~~ **dNKT** cells can shift the response from a destructive pro- inflammatory and cytotoxic environment towards an anti- inflammatory and protective environment (see Figure 3) and are critical for minimizing the damage caused by inflammatory responses in certain fibrotic and autoimmune diseases. Figure 3. iNKT and ~~type 2 NKT~~ **dNKT** cells have opposing roles in controlling inflammation (arrows in the left panel indicate activation and arrows in the right panel indicate inhibition). Repeated activation of iNKT cells can lead to chronic pulmonary diseases and are elevated in patients. Regulating iNKT cell activity has been observed to be therapeutic in animal models of IPF and activated iNKT cells accumulate in the lungs of IPF, NASH and SLE patients, as well as other chronic inflammatory, fibrotic, and autoimmune disease populations. Figure 4. Activated iNKT cells are increased in PBMC samples from IPF, ~~NASH~~ **MASH** and SLE patients compared to healthy subjects. Current IPF therapies slow the decline in lung function but do not improve overall survival. Regulating iNKT cell activity and their ability to promote macrophage polarization, TGF- beta production, and activation of myofibroblasts suggests they may reduce fibrosis progression and lead to improved survival outcomes in IPF. Activated iNKT cells are significantly upregulated in IPF patients and have the potential to be an important pharmacodynamic biomarker for these patients. We have observed that activated iNKT cells increase in ~~NASH~~ patients **with metabolic dysfunction- associated steatohepatitis (MASH)** as the disease progresses from healthy individuals to mild non- alcoholic fatty liver disease and advanced ~~NASH~~ **MASH** and believe iNKT may be a similar biomarker for IPF patients (see Figure 5). Figure 5. CXCR3 IFN- gamma activated iNKT cells increase in ~~NASH~~ **MASH** patients as disease progresses from healthy, mild to advanced disease. In models of pulmonary, renal, and hepatic fibrosis- including IPF, SLE, ~~NASH~~ **MASH** , ALD, DILI, and autoimmune hepatitis- iNKT cells play an important pathogenic role in mediating tissue damage by rapidly accumulating, becoming activated and secreting cytokines and chemokines for induction of a pro- inflammatory cascade that includes activation of the IL- 1beta inflammasome and neutrophil recruitment, differentiation and activation of pro- fibrotic myofibroblasts / hepatic stellate cells, collagen deposition and fibrosis. GRI has also identified several modulators of ~~type 2 NKT~~ **dNKT** cell activity, including cis- tetracosenoyl sulfatide (sulfatide), certain phospholipids, and GRI- 0124. GRI- 0803, as well as GRI' s library of over 500 compounds, are structurally related to GRI- 0124. In vivo administration of GRI- 0803 and GRI- 0124 activates ~~type 2 NKT~~ **dNKT** cells and inhibits the expansion of activated iNKT cells. Together, we believe these data support a model of iNKT inhibitors, such as GRI- 0621, and ~~type 2 NKT~~ **dNKT** modulators, such GRI- 0803, as well as GRI- 0124 and GRI- 0729, working together to balance inflammatory immune responses. Pulmonary Disease IPF is a rare life- threatening disease characterized by progressive fibrosis and abnormal scarring that destroys the structure and function of the lungs over time by blocking the movement of oxygen into the bloodstream, leading to their deterioration and destruction. The most common symptoms of IPF are shortness of breath and a dry persistent cough. Our Product Candidate Portfolio GRI- 0621 is an oral gel capsule formulation of an FDA- approved topical dermatology product, tazarotene (ethyl 6- [2- (4, 4- dimethylthiochroman- 6- yl) ethynyl] nicotinate), a synthetic RAR- beta and gamma- selective agonist and potent inhibitor of iNKT cells. Tazarotene is approved in topical formulations for psoriasis and acne and has been evaluated in over 1, 700 patients as an oral product dosed in subjects for up to 52- weeks. The Company is developing GRI- 0621 for the treatment of IPF. IPF background and market opportunity IPF is the most common and severe form of progressive pulmonary fibrosis, affecting approximately 140, 000 patients in the United States. Up to 40, 000 new cases are diagnosed in the United States each year, primarily affecting individuals between the ages of 65 and 70, and prevalence in the United States is expected to rise with an aging population. The median survival is between two to three years after diagnosis, and the average life expectancy for patients with confirmed IPF is between three and five years. Current treatments for IPF and their limitations Some IPF patients with mild or moderate symptoms are treated with either nintedanib, marketed as OFEV by Boehringer Ingelheim Pharmaceuticals, Inc., or pirfenidone, marketed as Esbriet by Genentech USA, Inc. These drugs have been shown to slow progression of decrease in lung function associated with IPF and deterioration of pulmonary function, but neither drug has been associated with improvements in overall survival, and both have been associated with significant side effects. It is estimated that over 60 % of patients dosed with nintedanib have diarrhea and approximately 14 % experience elevated levels of liver enzymes. Approximately 30 % of patients treated with pirfenidone have skin rash, and approximately 9 % experience photosensitivity, both of which can lead to dose reductions or discontinuations. Both agents have some efficacy in patients with more advanced disease, but high rates of discontinuations due to adverse events in these frailer patients limit their use. A survey of 290 physicians published by a third **-** party in 2017 found that over half of IPF patients are not being treated with either agent for multiple reasons, including physicians not having sufficient confidence in clinical benefit and concerns about safety. A retrospective cohort analysis of prescription records conducted by researchers at the Mayo Clinic and presented in 2019 found that the adoption of pirfenidone and nintedanib by IPF patients was approximately 10 % for each therapy, supporting the earlier observation that the majority of IPF patients are not actively being treated. Despite this, total worldwide sales of pirfenidone and nintedanib in ~~2019~~ **2022** were ~~over~~ $ ~~1~~ **4** . ~~2~~ **3** billion **combined** ~~and $ 1. 6 billion, respectively~~ . Our Solution- GRI- 0621 We are developing GRI- 0621 as an oral gel capsule formulation to treat IPF patients. GRI- 0621 is differentiated from current IPF therapies because it is designed to reset the dysfunctional immune response driving disease by inhibiting the activity of iNKT cells, as opposed to targeting a symptom of the disease that is downstream of the dysregulated immune response. GRI- 0621 has been evaluated as an oral formulation in approximately 1, 700 psoriasis, acne, and liver disease patients and in those patient populations and studies, the molecule was well **-** tolerated with typical reported adverse events associated with hypervitaminosis A (headache, back pain, foot pain, cheilitis, hyperglycemia, arthralgia, myalgia, joint disorder, nasal dryness, dry skin, rash, and dermatitis). In preclinical studies, animals lacking iNKT cells were observed to be protected from fibrosis in models of IPF,

~~NASH~~ **MASH** , ALD, autoimmune liver disease, and DILI. Similarly, inhibiting the activity of iNKT cells can protect and / or treat animals from developing fibrosis. Fibrosis is a complex dynamic process involving several signaling molecules, differentiation pathways, and multiple cell types in different tissues. Thus, when the wound repair mechanism goes awry due to chronic inflammation / injury, this results in tissue scarring, stiffness and eventually malfunction. Despite its complexity, scientific literature suggests that there are common biological mechanisms that drive fibrosis in different tissues such as lung, liver, and kidney. In our preclinical studies, GRI- 0621 administration in animal models of hepatic fibrosis was observed to inhibit secretion of pro- inflammatory cytokine secretion by iNKT cells (see Figure 6) and maturation and activation of pro-inflammatory Kupffer cells and pro- fibrogenic myofibroblasts / hepatic stellate cells (see Figures 7 and 10). Figure 6. GRI-0621 observed to inhibit in vivo expansion and activation of iNKT cells and inhibits pro- inflammatory cytokines in animal models of fibrosis. Figure 7. GRI- 0621 observed to inhibit Kupffer cells and the activation and maturation of myofibroblasts / hepatic stellate cells. Consistently, iNKT knock- out (KO) animals that lack iNKT cells were observed to fail to upregulate pro-fibrogenic genes relative to wild type animals (WT) in models of fibrosis (see Figure 8). Figure 8. Inhibition of the key fibrogenic genes, including CTGF, observed in the iNKT- deficient animal model of fibrosis. One of the most important signaling molecules driving fibrogenesis is TGF- beta. In our models of pulmonary and hepatic, and renal fibrosis, functional inactivation of iNKT cells with iNKT inhibitors or ~~type 2 NKT~~ **dNKT** cell activators led to a significant inhibition of this key mediator of fibrosis (see Figure 9). Figure 9. Inhibition of iNKT cells significantly reduced TGF- beta in models of pulmonary and hepatic fibrosis. In our preclinical studies, a reduction in pro- inflammatory cytokines, Kupffer cells, activated myofibroblasts, pro- fibrogenic gene expression and the critical soluble mediator of fibrosis, TGF- beta, resulted in reduced collagen deposition and fibrosis in liver and lung models of fibrosis (see Figures 10, 11, and 12). Figure 10. Hepatic inflammation & steatosis (H & E), myofibroblast activation (~~“~~anti- SMA ~~”~~) and fibrosis (~~“~~Sirius Red ~~”~~) were inhibited (left histology panels and upper bar graphs) as well as IFN- gamma, TNF- alpha, and IL- 2 (lower bar graphs) following GRI- 0621 administration in the choline- deficient L- amino- defined model of ~~NASH~~ **MASH** . Figure 11. iNKT inhibitors observed to prevent inflammation, inflammatory cytokines, and TGF- beta in a bleomycin model of pulmonary fibrosis. Figure 12. GRI-0621 observed to ~~inhibit~~ **improve** lung ~~inflammation~~ **injury** (H & E **), myofibroblast activation (a- SMA**) and fibrosis (Mason’ s Trichrome **and Sirius Red**) in a bleomycin **treatment** model of pulmonary fibrosis. GRI- 0621 Pilot Phase 2a Trial in Hepatically Impaired Subjects We evaluated GRI- 0621 in a pilot Phase 2a trial in hepatically impaired chronic liver disease patients. The study was originally intended to evaluate 60 patients, but we made the administrative decision to halt the study after enrolling 14 patients due to recruitment challenges and updated guidance from the FDA regarding the design of **non-alcoholic steatohepatitis (** NASH **)** clinical studies. In this limited number of patients, GRI- 0621 was observed to be well **-** tolerated and showed improvements in liver function tests, serum CK- 18, and in iNKT cell activity, however, the study was underpowered to meet its endpoints with statistical significance. Adverse events were generally mild and consistent with ~~RARb-~~ **RAR** ~~g-~~ **- beta and gamma** agonism (see table below). ALL- CAUSEPLACEBO (n = 4) GRI- 0621 4. 5mg (n = 4) GRI- 0621 6. 0mg (n = 5) SERIOUS TEAEs000GRADE 1 TEAEs000GRADE 2 TEAEs000GRADE 3 / 4 / 5 TEAEs000TREATMENT RELATEDCHELITIS000NASEAU000DRY SKIN000PURITIS000HEADACHE000MYLAGIA000HYPERTENSION001 * GASTROENTERITIS000TONSILITIS001 * CREATINE PHOSPHOKINASE000LACTATE DEHYDROGENASE000POTASSIUM000 * Grade 2 treatment emergent adverse events (TEAE) GRI- 0621 Manufacturing We rely on third- party contract manufacturers to manufacture GRI- 0621 for preclinical studies and clinical trials, and do not own manufacturing facilities for producing any preclinical study or clinical trial product supplies. We rely on a limited number of suppliers for drug product and engage a single manufacturer to produce our formulated GRI- 0621 drug product for clinical studies, as is standard industry practice in early to mid- stage clinical development. If these suppliers are unable to supply to us in the quantities we require, or at all, or otherwise default on their supply obligations to us, we may not be able to obtain alternative supplies from other suppliers on acceptable terms, in a timely manner, or at all. In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturer or manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. GRI- 0621 Phase 2a Trial in Patients with IPF In December 2023 we commenced enrollment for our Phase 2a trial. This trial will be a twelve- week, multicenter, multinational, randomized, placebo-controlled trial in approximately 36 patients with IPF. A 4. 5 mg dose will be compared to placebo over twelve weeks of treatment in subjects with a confirmed diagnosis of IPF on background therapy. Subjects will complete a screening visit to evaluate their medical history, present condition, laboratory assessments, comorbidities, and concomitant medications. Based on these findings, subjects will be randomly assigned to one of two treatment arms: 4. 5 mg of GRI- 0621 or placebo in a 2: 1 randomization. Weekly visits out to twelve weeks will evaluate safety, pharmacokinetics, and efficacy / mechanism of action of GRI- 0621 as assessed by the activation of iNKT cells from both blood at weeks 6 and 12 and bronchi- alveolar lavage fluid at week 12. As a secondary endpoint, various biomarkers will also be evaluated to support the mechanism of action of GRI- 0621. Subjects will be followed for at least two weeks after completion of dosing. ~~This trial should take approximately six months to recruit the required number of subjects and be completed within approximately ten months of first subject’ s first visit.~~ Topline data from this trial should be available in the ~~second half~~ **third quarter** of ~~2024~~ **2025** . Final results from this trial will be used to determine dose, safety sample size, clinically relevant endpoints, and duration in communication with the FDA in designing the registration program moving forward. GRI- 0803 for the Treatment of Lupus Nephritis Related to Systemic Lupus Erythematosus Systemic Lupus Erythematosus Disease Background SLE is the most common type of lupus, affecting between

160, 000- 200, 000 patients in the United States, and as many as 24, 000 people in the United States are diagnosed with the disease each year. SLE predominantly affects women and often starts between the ages of 15 and 44. SLE is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels. There is no cure for lupus, but medical interventions and lifestyle changes can help control it. While people of all races can have the disease, African American women have a three- times higher number of new cases than white, non- Hispanic women. African American women tend to develop the disease at a younger age than white, non- Hispanic women and develop more serious and life- threatening complications. It is also more common in women of Hispanic, Asian and Native American descent. Adherence to treatment regimens is often a problem, especially among young women of childbearing age. Because SLE treatment may require the use of strong immunosuppressive medications that can have serious side effects, female patients must stop taking the medication before and during pregnancy to protect unborn children from harm. Current Treatments for SLE, their Limitations and Lupus Nephritis The treatment and management of SLE depends on disease severity and disease manifestations. Hydroxychloroquine plays a central role in the long- term treatment of SLE and is the cornerstone of SLE therapy. Corticosteroids, nonsteroidal anti- inflammatory drugs, and immunosuppressive agents (e. g., azathioprine, cyclophosphamide, cyclosporine, methotrexate, and mycophenolate mofetil) have also been used in the treatment and management of SLE. These treatments are only modestly effective and present safety and / or immune suppression concerns with prolonged use. The B cell- depleting antibody rituximab, while not approved for treatment of SLE, appears to be beneficial in certain subsets of patients. Two targeted therapies for SLE have been approved by the FDA in the past 50 years, belimumab and anifrolumab. In 2011, the FDA approved belimumab (Benlysta ®), an antibody that targets B lymphocyte stimulator, for the treatment of mild to moderate SLE in combination with standard therapy, providing additional clinical validation of the therapeutic benefit of B cell- targeted therapy for autoimmune diseases. However, the modest therapeutic benefit of Benlysta ® and delayed onset of disease intervention indicate the need for additional therapeutic strategies to inhibit overactive B cells. In 2021, the first- in- class type 1 interferon receptor antibody, anifrolumab, the first new drug for the disease in a decade, was approved for adults with moderate to severe disease who are receiving standard therapy. Lupus nephritis is a common manifestation of SLE and can lead to irreversible renal impairment. This disease is complex, heterogeneous and involves multiple cell types as well as immune and non- immune mechanisms. Disease progression is characterized by glomerular injury, inflammation, cellular infiltration, and fibrosis. The deposition of immune complexes leads to inflammasome and type I interferon mediated pathways contributing to endothelial dysfunction in conjunction with complement- mediated injury owing to pathogenic antibodies. Our Solution- GRI- 0803 Scientific studies have suggested that iNKT plays an important pathogenic role in kidney diseases, including acute kidney injury, ischemic reperfusion injury and lupus nephritis. Accordingly, iNKT cells were activated in peripheral blood of lupus patients (see Figure 4, above) and in spontaneous models of lupus. Notably, activation of ~~type 2 NKT~~ **dNKT** leads to a dendritic cell- mediated inhibition of iNKT cells. In our preclinical studies, a ~~type 2 NKT~~ **dNKT** activating molecule, GRI- 0803, was observed to inhibit both murine and human iNKT cells. Oral administration of GRI- 0803, a ~~type 2 NKT~~ **dNKT** activating molecule, was observed to inhibit lupus nephritis and to significantly improve overall survival. Following a weekly oral administration of GRI- 0803 in a spontaneous model of lupus nephritis significant inhibition of pro- inflammatory cytokines, including IL- 17 and IL- 6 (see Figure ~~12~~ **13**) was observed. Other fibrogenic molecules, including TGF- beta, were also observed to be inhibited leading to blocking of collagen deposition and renal fibrosis (see Figure ~~13~~ **14**). This was observed to be accompanied by inhibition of cellular infiltration (including B cells and T cells) into the kidney and glomerular pathology. Furthermore, following GRI- 0803 administration, significant inhibition of pathogenic anti- dsDNA antibodies, and proteinuria as measured in urine (see Figures ~~13~~ **15** and ~~14~~ **16**) was observed. Additionally, GRI- 0803 was observed to block activation of plasmacytoid dendritic cells and type I interferon signaling pathway genes involved in renal injury. Inhibition of renal disease was reflected in the improvement of overall survival of proteinuria- free animals. Lipocalin 2 (LCN2) is a glycoprotein secreted by several immune cells and promotes pro- inflammatory immune responses in autoimmune diseases and suggested to be an indicator of the severity of lupus nephritis. Interestingly, among other inflammatory genes, significant inhibition of LCN2 expression in the kidney was observed in animals orally treated with GRI- 0803 in comparison to that in the control group (see Figure ~~12~~ **13**). Figure ~~12~~ **13** . Inhibition of several key pro- inflammatory, fibrotic and kidney disease promoting genes in a spontaneous lupus model observed following oral administration of GRI- 0803. Figure ~~13~~ **14** . GRI- 0803 administration observed to inhibit inflammatory cellular infiltration (H & E), glomerular pathology (~~“~~PAS ~~”~~), and kidney fibrosis (~~“~~Trichrome ~~”~~) in a spontaneous lupus model. Figure ~~14~~ **15** . Observed inhibition anti- dsDNA antibodies in serum and increased overall survival in a lupus model following treatment with GRI- 0803. Figure ~~15~~ **16** . Significant inhibition of proteinuria in urine and spontaneously occurring lupus nephritis observed in animals orally treated with GRI- 0803. GRI- 0803 Manufacturing We rely on third- party contract manufacturers to manufacture GRI- 0803 for preclinical studies, and do not own manufacturing facilities for producing any preclinical study product supplies. We rely on a single or limited number of suppliers for drug product and engage a single manufacturer to produce our formulated GRI- 0803 drug product for clinical studies, as is standard industry practice in early to mid- stage clinical development. If these suppliers are unable to supply to us in the quantities we require, or at all, or otherwise default on their supply obligations to us, we may not be able to obtain alternative supplies from other suppliers on acceptable terms, in a timely manner, or at all. In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturer or manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. GRI- 0803 Phase 1 Trial We plan to initiate a

Phase 1 trial upon completion of the toxicology program for GRI- 0803. Assuming positive results, we anticipate filing an IND in ~~the first half of 2024~~ **2025** . The Single Ascending Dose (SAD) trial will be run in healthy volunteers. Up to six doses will be evaluated in cohorts of 12 subjects with 10 receiving a dose of GRI- 0803 and two receiving placebo. The safety in each cohort will be evaluated with an Independent Safety Review Board (ISRB) along with the GRI clinical management. After completion of the first cohort, subsequent cohorts will begin within two weeks of dosing the previous cohort. Pharmacokinetics and safety will be the primary endpoint of the SAD trial. The completion of this trial should take approximately three months from when the first cohort is dosed. The Multiple Ascending Dose (MAD) trial will begin upon the completion of Dose 3 in the SAD trial based on the recommendation of the ISRB. The MAD trial will examine four doses of GRI- 0803 with doses dependent on the results of the SAD. A total of 10 subjects will be in each cohort: eight on GRI- 0803 and two on placebo. Cohorts will be dosed for four weeks with two weeks of safety follow up post dosing with the first two cohorts being in healthy subjects and the two highest doses will be completed in patients with SLE. Safety and multi- dose pharmacokinetics will be the primary endpoint of the MAD trial. Exploratory outcomes will be examined in the third and fourth cohorts and will include several biomarkers (e. g., cytokines) as well as NKT cell activation markers. ~~The MAD trial should take approximately five months to complete with topline results available late in the fourth quarter of 2024.~~ Competitive Landscape The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, the expertise of our management team, clinical capabilities, research and development experience and scientific knowledge provide us with competitive advantages, we face increasing competition from many different sources, including biotechnology and biopharmaceutical companies, academic institutions, governmental agencies, and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. There are several large biotechnology and biopharmaceutical companies that are currently pursuing the development of products for the treatment of conditions GRI is also targeting, or may target in the future, including IPF, SLE, MS, UC, PSC and ~~NASH~~ **MASH** . While we know of no other companies currently in clinical development targeting NKT cells as a method of treating any of the above conditions, companies that we are aware of that are targeting the treatment of these diseases include large companies with significant financial resources such as: IPF- AstraZeneca PLC, Boehringer Ingelheim International GmbH, Bristol- Myers Squibb Co., **Eli Lilly** and **Company, Genentech,** ~~Novartis AG. Additional smaller companies with significant resources include Avalyn Pharma~~ Inc., **GlaxoSmithKline plc** ~~Bellerophon Therapeutics, Inc.~~ , Endeavor Biomedicines, Inc., ~~Horizon Therapeutics Public Limited Company~~ **Guangzhou JOYO Pharma Co., Ltd., InSilico Medicine Hong Kong Ltd.** , Pliant Therapeutics, Inc., Suzhou Zelgen Biopharmaceuticals Co. Ltd., United Therapeutics Corp **.** and Vicore Pharma Holding AB. SLE- Astellas Pharma Inc., AstraZeneca PLC, Aurinia Pharmaceuticals Inc., Biogen Inc., **Bristol- Myers Squibb Co., Gilead Sciences, Inc.,** GlaxoSmithKline ~~PLC~~ **plc** , Johnson & Johnson, Nektar Therapeutics, **Novartis AG, Pfizer Inc.,** Roche Holding AG ~~and~~ **,** Sanofi ~~SA~~ **S. A. and UCB S. A** . Additional smaller companies with significant resources include Anthera Pharmaceuticals, Inc., Aurinia Pharmaceuticals Inc., ImmuPharma PLC, Kezar Life Sciences, Inc., Vera Therapeutics, Inc. and Viela Bio, Inc. ~~PSC- Albireo Pharma, Inc., Avolynt Inc., Calliditas Therapeutics AB, Cascade Pharmaceuticals, Inc., Chemomab Therapeutics Ltd., CymaBay Therapeutics, Inc., Dr. Falk Pharma GmbH, Galmed Pharmaceuticals Ltd., Gannex Pharma Co. Ltd., Genfit Corp., Gilead Sciences, Inc., HighTide Therapeutics Inc., Immunic, Inc., Invea Therapeutics, Inc., LISCure Biosciences Inc., Mirum Pharmaceuticals, Inc., Morphic Holding, Inc., Pliant Therapeutics, Inc., Selecta Biosciences Inc., Sirnaomics, Inc. and Qing Bile Therapeutics. NASH- AstraZeneca PLC, Eli Lilly and Company, Gilead Sciences, Inc., Merck & Co. Inc., Novo Nordisk A / S, Novartis AG, Pfizer Inc. and Roche Holding AG. Additional smaller companies with significant resources include: Enanta Pharmaceuticals Inc., Ionis Pharmaceuticals Inc., NGM Biopharmaceuticals Inc., Pliant Therapeutics, Inc., Terns Pharmaceuticals, Inc. and 89bio, Inc. MS- Biogen Inc., Bristol- Myers Squibb Co., EMD Serono, Inc., Johnson & Johnson, Merck & Co. Inc., Novartis AG, Sanofi, Teva Pharmaceuticals Industries LTD and Roche Holding AG. UC- AbbVie Inc., AstraZeneca PLC, Bristol- Myers Squibb Co., Eli Lilly and Company, Gilead Sciences, Inc., Janssen Biotech, Inc., Johnson & Johnson, Pfizer Inc., Merck & Co. Inc., Millennium Pharmaceuticals, Inc., Protagonist Therapeutics, Inc., Roche Holding AG, and Takeda Pharmaceutical Co Ltd.~~ The key competitive factors affecting the success of our product candidates are likely to be efficacy, safety, cost, and convenience. Many of our competitors, either alone or with their collaborators, have significantly greater resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing, and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Additional mergers and acquisitions may result in even more resources being concentrated in our competitors. We strive to protect the proprietary technology and information commercially or strategically important to our business. We seek to obtain and maintain, patent rights intended to cover the technologies incorporated into, or used to produce, our therapeutic candidates, the compositions of matter of our therapeutic candidates and their methods of use and manufacture, as well as other inventions that are important to our business. We also seek to obtain strategic or commercially valuable patent rights in the United States and other jurisdictions. To cover our proprietary technologies and our current pipeline of proprietary products and related methods, such as methods of use, we have filed patent applications representing six patent families. As of February ~~15~~ **28** , ~~2024~~ **2025** , our patent estate included 12 issued United States patents, ~~2~~ **two** United States pending non- provisional patent applications, ~~65~~ **75** issued foreign patents and ~~16~~ **10** foreign patent applications currently pending in various foreign jurisdictions. Specifically, we own one patent family with claims directed to GRI- 0621, and related methods of using the same to treat diseases, e. g. inflammatory conditions. Three United States and ~~20~~ **22** foreign patents (Australia, Brazil, Canada, China, Europe (validated in nine countries), Hong

Kong, Japan, South Korea, Mexico, and Russia) were granted in this family. Patent applications in this family are pending in multiple jurisdictions, including, for example, the European Patent Organization ~~,~~ **and** China ~~, Japan, and Korea~~ . Patents in this patent family are expected to expire in 2032, absent any patent term adjustments or extensions. We also own one patent family with claims directed to GRI- 0803 and related methods of using the same to treat diseases. Three United States and nine foreign patents (Canada, Europe (validated in seven countries), and Hong Kong) were granted in this family. Patent applications in this family are pending in the United States and European Patent Organization. Patents in this patent family are expected to expire in 2032, absent any patent term adjustment or extension. Additionally, we own one patent family relating to GRI- 0729 and related methods of using the same to treat diseases. Four United States and 13 foreign patents (Canada, Europe (validated in 11 countries), and Hong Kong) have been granted in this family. Patents in this patent family are expected to expire in 2032, absent any patent term adjustment or extension. We also own one patent family with claims directed to GRI- 0124 and related methods of using the same to treat diseases. Fourteen foreign patents (Taiwan, Australia, China, Europe (validated in seven countries), Hong Kong, Israel, Mexico and Russia) were granted in this family. Patent applications in this family are pending, for example, in the United States, United Arab Emirates, Brazil, China, Japan, Russia, Canada, Hong Kong and South Korea. Patents in this patent family are expected to expire in 2035, absent any patent term adjustment or extension. We continually assess and refine our intellectual property strategy as we develop new technologies and therapeutic candidates. As our business evolves, we may, among other activities, file additional patent applications in pursuit of our intellectual property strategy, to adapt to competition or to seize potential opportunities. The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non- provisional patent application. However, the term of United States patents may be extended for delays incurred due to compliance with the FDA requirements or by delays encountered during prosecution that are caused by the United States Patent and Trademark Office (USPTO). For example, the Hatch- Waxman Act, permits a patent term extension for FDA- approved drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our therapeutic candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those therapeutic candidates. We intend to seek patent term extensions in any jurisdiction where these are available and where we also have a patent that may be eligible; however there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Further, we expect to rely on data exclusivity, market exclusivity, patent term adjustment and patent term extensions when available. Government Regulation and Product Approval Government authorities in the United States ~~,~~ at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, clinical trials, testing, manufacture (including any manufacturing changes), authorization, pharmacovigilance, adverse event reporting, recalls, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products and product candidates such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. United States Government Regulation In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions brought by the FDA and the Department of Justice (DOJ), or other governmental entities, such as the FDA' s refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil and / or criminal penalties. The process required by the FDA before a new drug may be marketed in the United States generally involves the following: • completion of nonclinical and preclinical studies, such as laboratory tests, potentially animal studies and formulation studies, in compliance with FDA regulations for Good Laboratory Practices (GLPs) and other applicable regulations; • submission to the FDA of an IND, which must become effective before human clinical trials may begin; • approval by an IRB covering each clinical site before a trial may be initiated; • performance of adequate and well-controlled human clinical trials in accordance with good clinical practices (GCPs) to establish the safety and efficacy of the proposed drug product for each indication; • submission to the FDA of an NDA with payment of application user fees, if applicable, and FDA acceptance of that NDA; • satisfactory completion of an FDA advisory committee review, if applicable; • satisfactory completion of an FDA pre- approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices (cGMPs) and to assure that the facilities, methods and controls are adequate to preserve the drug' s identity, strength, quality and purity; • satisfactory completion of audits of clinical trial sites conducted by FDA to assure compliance with GCPs and the integrity of clinical data; and • FDA review and approval of the NDA. Preclinical Studies Preclinical or nonclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as potential animal studies to assess potential safety and efficacy. The Consolidated Appropriations Act for 2023, signed into law on December 29, 2022, (P. L. 117- 328) amended the FDCA to specify that nonclinical testing for drugs may, but is not required to, include in vivo animal testing. According to the amended language, a sponsor may fulfill nonclinical testing requirements by completing various in vitro assays (e. g., cell- based assays, organ chips, or microphysiological systems), in silico studies (i. e., computer modeling), other human or non- human biology- based tests (e. g., bioprinting), or in vivo animal tests. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with GLP regulations and the U. S. Department of Agriculture' s Animal Welfare

Act. A drug sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available ex- U. S. clinical data or relevant literature, among other things, to the FDA as part of an IND. Some nonclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial if the clinical trial is not being conducted in accordance with the IRB' s requirements or if the product candidate has been associated with unexpected serious harm to patients. Clinical Trials Clinical trials involve the administration of the IND to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial (unless the consent requirement has been waived by an IRB) along with the requirement to ensure that the data and results reported from the clinical trials are credible and accurate. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the criteria for determining subject eligibility, the dosing plan, the parameters to be used in monitoring safety, the procedure for timely reporting of adverse events, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB must review and approve the plan for any clinical trial before it commences. Information about certain clinical trials and clinical trial results must be submitted within specific timeframes to the National Institutes of Health for public dissemination on the Clinicaltrials. gov registry. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non- compliant party from receiving future grant funds from the federal government. The government has brought enforcement actions against clinical trial sponsors that fail to comply with such requirements. Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined: Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness. During Phase 1 clinical trials, sufficient information about the investigational drug' s pharmacokinetics and pharmacological effects may be obtained to permit the design of well- controlled and scientifically valid Phase 2 clinical trials. Phase 2: The product candidate is administered to a larger, but still limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dosage tolerance and optimal dosage. Phase 2 clinical trials are typically well- controlled and closely monitored. Phase 3: The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well- controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk- benefit profile of the product, and to provide adequate information for the labeling of the product. Phase 3 clinical trials usually involve a larger number of participants than a Phase 2 clinical trial. Post- approval trials, sometimes referred to as " Phase 4 " clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of " Phase 4 " clinical trials. Human clinical trials are inherently uncertain, and Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Moreover, a given clinical trial may combine the elements of more than one phase and a company' s designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted and reviewed. A pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate' s safety and efficacy such that it can be used, alone or with other pivotal or non- pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well- controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need. In recent years, the FDA has been increasingly willing to exercise regulatory flexibility when determining the types, amount, and timing of data submissions to support the demonstration of a " substantial evidence of effectiveness, " which is the legal standard applicable to new drug approvals and is discussed further below. Congress also recently amended the FDCA in order to require sponsors of a Phase 3 clinical trial, or other " pivotal study " of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must include the sponsor' s diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Sponsors must submit a diversity action plan to the FDA by the time the sponsor submits the relevant clinical trial protocol to the agency for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. If the FDA objects to a sponsor' s diversity action plan or otherwise requires significant changes to be made, it could potentially delay initiation of the relevant clinical trial. Interactions with FDA During the Clinical Development Program Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (pre- IND meeting), at the end of Phase 2

clinical trial (EOP2 meeting) and before an NDA is submitted (pre- NDA meeting). Meetings at other times may also be requested. These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development. For example, at an EOP2, a sponsor may discuss its Phase 2 clinical results and present its plans for the pivotal Phase 3 clinical trial (s) that it believes will support the approval of the new product. Such meetings may be conducted in person, via teleconference / videoconference or written response only with minutes reflecting the questions that the sponsor posed to the FDA and the agency' s responses. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute recommendations and / or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and / or advice. Nonetheless, from a practical perspective, a sponsor' s failure to follow the FDA' s recommendations for design of a clinical program may put the program at significant risk of failure. Acceptance of NDAs Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product' s chemistry, manufacturing, controls, safety updates, patent information, abuse information and proposed labeling, are submitted to the FDA as part of an application requesting approval to market the product candidate for one or more indications. Data may come from company- sponsored clinical trials intended to test the safety and efficacy of a product' s use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug product. The fee required for the submission and review of an application under the Prescription Drug User Fee Act (PDUFA) is substantial, and the sponsor of an approved application is also subject to an annual program fee assessed based on eligible prescription drug products. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review **. Congress is required to re- authorize the agency' s user fee programs every five years, and current legislative provisions supporting the PDUFA program are set to expire on September 30, 2027** . The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, the FDA' s regulations state that an application " shall not be considered as filed until all pertinent information and data have been received " by the FDA. In the event that the FDA determines that an application does not satisfy this standard, it will issue a Refuse to File (RTF) determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Review of NDAs After the submission is accepted for filing, the FDA begins an in- depth substantive review of the application. ~~The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMPs.~~ Under the **current PDUFA** goals and policies agreed to by the FDA ~~under PDUFA~~ , the ~~FDA~~ **agency** has ten months from the filing date in which to complete its initial review of a standard application that is a new molecular entity, and six months from the filing date for an application with " priority review. " The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, the NDA review process can be very lengthy and it is not uncommon for FDA review of an application to extend beyond the PDUFA target action date. Most innovative drug products (other than biological products) obtain FDA marketing approval pursuant to an NDA submitted under Section 505 (b) (1) of the FDCA, commonly referred to as a traditional or " full NDA. " In 1984, with passage of the Hatch- Waxman Act that established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs based on an innovator or " reference " product, Congress also enacted Section 505 (b) (2) of the FDCA, which provides a hybrid pathway combining features of a traditional NDA and a generic drug application. Section 505 (b) (2) enables the applicant to rely, in part, on the FDA' s prior findings of safety and efficacy data for an existing product, or published literature, in support of its application. Section 505 (b) (2) NDAs may provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products that would require new clinical data to demonstrate safety or effectiveness. Section 505 (b) (2) permits the filing of an NDA in which the applicant relies, at least in part, on information from studies made to show whether a drug is safe or effective that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. A Section 505 (b) (2) applicant may eliminate or reduce the need to conduct certain preclinical or clinical studies, if it can establish that reliance on studies conducted for a previously- approved product is scientifically appropriate. The FDA may also require companies to perform additional studies or measurements, including nonclinical and clinical studies, to support the change from the approved product. The types of studies and extent of data necessary to establish the safety and / or effectiveness of the new product, such as the effects of changing the drug' s route of administration from topical to oral, are scientifically driven and determined on a case- by- case basis. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication for which the Section 505 (b) (2) NDA applicant has submitted data. In connection with its review of an application, the FDA will typically submit information requests to the applicant and set deadlines for responses thereto. The FDA will also conduct a pre- approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMPs and are adequate to assure consistent production of the product within required specifications.

The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. To ensure compliance with cGMPs and GCPs by its employees and third- party contractors, an applicant may incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control. The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCPs and the FDA is able to validate the data through an on- site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical trials, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the United States population and United States medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on- site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA may refer an application, including applications for novel product candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval. Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the sponsor interprets the same data. The FDA may also re- analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process or delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. The FDA also may require submission of a risk evaluation and mitigation strategy (REMS) if it determines that a REMS is necessary to ensure that the benefits of the drug product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans and / or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case- by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS. In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation. Decisions on NDAs The FDA reviews an ~~applicant~~ **application** to determine, among other things, whether the product is safe and whether it is effective for its intended use (s), with the latter determination being made on the basis of substantial evidence. The term " substantial evidence " is defined under the FDCA as " evidence consisting of adequate and well- controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. " The FDA has interpreted this evidentiary standard to require at least two adequate and well- controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that " If [the FDA] determines, based on relevant science, that data from one adequate and well- controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the FDA may consider such data and evidence to constitute substantial evidence. " This modification to the law recognized the potential for the FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, the FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. In September 2023, the agency supplemented and expanded the recommendations in the 2019 " substantial evidence of effectiveness " draft guidance with a second draft guidance entitled " Demonstrating Substantial Evidence of Effectiveness Based on One Adequate and Well- Controlled Clinical Investigation and Confirmatory Evidence. " The second document complements the first by providing further detail on the use of data drawn from one or more sources (e. g., clinical data, mechanistic data, animal data) in order to support the results of one adequate and well- controlled clinical investigation and provides examples of types of data that could be considered confirmatory evidence. Due to the case- by- case nature of such determinations, the FDA continues to emphasize the need for sponsors to engage early with the agency if they intend to establish substantial evidence of effectiveness with one adequate and well- controlled clinical investigation plus confirmatory evidence. After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter (CRL) or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This " benefit- risk " assessment is informed by the extensive body of evidence about the product' s safety and efficacy in the NDA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real- world use of the product in the post- market setting; and

whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an " action package, " which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision. A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial (s) and / or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an additional six- month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e. g., patient population, indication) described in the FDA- approved labeling. Further, depending on the specific risk (s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post- approval trials, including Phase 4 clinical trials, be conducted to further assess a product' s safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post- marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval. Special FDA Expedited Review Programs The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life- threatening disease or condition. These programs include fast track designation, breakthrough therapy designation, and priority review designation. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life- threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA' s review team and may allow for a rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. In addition, fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process. In addition, with the enactment of the FDA Safety and Innovation Act (FDASIA) in 2012, Congress created a new regulatory program for therapeutic candidates designated by the FDA as " breakthrough therapies " upon a request made by the IND sponsors. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA must take certain actions with respect to breakthrough therapies, such as holding timely meetings with and providing advice to the product sponsor, intended to expedite the development and review of an application for approval of a breakthrough therapy. Finally, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case- by- case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment- limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA' s goal for taking action on a marketing application from ten months to six months for an NDA for a new molecular entity from the date of filing. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, breakthrough therapy designation and priority review do not change the standards for approval and may not ultimately expedite the development or approval process. Accelerated Approval Pathway In addition, a product studied for its safety and effectiveness in treating serious or life- threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, meaning that it may be approved on (i) the basis of adequate and well- controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or (ii) on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) and that is reasonably likely to predict an effect on IMM or other clinical benefits, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post- marketing studies to verify and describe the predicted effect on IMM or other clinical endpoints, and the drug may be subject to expedited withdrawal procedures. Drugs granted accelerated approval

must meet the same statutory standards for safety and effectiveness as those granted traditional approval. All promotional materials for drug products being considered and approved under the accelerated approval program are subject to prior review by the FDA. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long- term clinical benefit of a drug. The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit. The accelerated approval pathway is usually contingent on a sponsor' s agreement to conduct, in a diligent manner, additional post- approval confirmatory studies to verify and describe the drug' s clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post- marketing compliance requirements, including the completion of Phase 4 or post- approval clinical trials to confirm the effect on the clinical endpoint. In addition, as part of the Consolidated Appropriations Act for 2023, Congress provided FDA additional statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval. Under these amendments to the FDCA, the agency may require a sponsor of a product granted accelerated approval to have a confirmatory trial underway prior to approval. The sponsor must also submit progress reports on a confirmatory trial every six months until the trial is complete, and such reports will be published on FDA' s website. Failure to conduct required post- approval studies, or to confirm the predicted clinical benefit of the product during post- marketing studies, would allow the FDA to withdraw approval of the drug. Congress also recently amended the law to give FDA the option of using expedited procedures to withdraw product approval if the sponsor' s confirmatory trial fails to verify the claimed clinical benefits of the product. All promotional materials for drug products being considered and approved under the accelerated approval program are subject to prior review by the FDA. Prior to the recent statutory amendments enacted by Congress, several oncology sponsors voluntarily withdrew specific indications for their drug products that were being marketed pursuant to accelerated approval. More recently, in February 2024 the FDA announced its first use of the law' s amended procedures to withdraw an accelerated approval following the drug' s confirmatory study failing to verify clinical benefit. Scrutiny of the accelerated approval pathway is likely to continue in the coming years and may lead to further legislative and / or administrative changes in the future. Post- Approval Requirements Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. Certain modifications to the product, including changes in indications or manufacturing processes or facilities, may require the applicant to develop additional data or conduct additional preclinical studies and clinical trials to support the submission to FDA. As previously noted, there also are continuing, annual user fee requirements for any marketed products, as well as new application fees for supplemental applications with clinical data. The FDA may impose a number of post- approval requirements as a condition of approval of an NDA. For example, the FDA may require post- marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product' s safety and effectiveness after commercialization. In addition, FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMPs include requirements relating to the organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and some state agencies and are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other laws. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting and documentation requirements upon the sponsor and any third- party manufacturers. Accordingly, manufacturers must continue to expend time, money, and effort in production and quality control to maintain compliance with cGMPs and other aspects of quality control and quality assurance. The FDA strictly regulates the marketing, labeling, advertising and promotion of drug products that are placed on the market. A product cannot be commercially promoted before it is approved, and approved drugs may generally be promoted only for their approved indications and for use in patient populations described in the product' s approved labeling. Promotional claims must also be consistent with the product' s FDA- approved label, including claims related to safety and effectiveness. The government closely scrutinizes the promotion of prescription drugs in specific contexts such as direct- to- consumer advertising, industry- sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Although physicians may prescribe legally available products for off- label uses, manufacturers may not market or promote such uses. The FDA has recently published a draft guidance outlining modernized recommendations for how drug manufacturers can share truthful, scientifically sound, and clinically relevant information on unapproved uses with health care providers. Later discovery of previously unknown problems with a product, including adverse

events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences of regulatory non- compliance include, among other things: • restrictions on, or suspensions of, the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls; • interruption of production processes, including the shutdown of manufacturing facilities or production lines or the imposition of new manufacturing requirements; • fines, warning letters or other enforcement letters or clinical holds on post-approval clinical trials; • mandated modification of promotional materials and labeling and the issuance of corrective information; • refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals; • product seizure or detention, or refusal to permit the import or export of products; • injunctions or the imposition of civil or criminal penalties; or • consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs. In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA) which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. **The** ~~More recently, the~~ Drug Supply Chain Security Act (the DSCSA) ~~,~~ was enacted **in 2013** with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandated ~~phased-in~~ and resource- intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10- year period that was designed to culminate in November 2023. However, the FDA announced a one- year " stabilization period " until November 2024 **, followed by trading partner- specific exemptions through specified dates in 2025** , to accommodate additional time that trading partners in the pharmaceutical supply chain needed in order to fully implement DSCSA requirements for electronic drug tracing at the package level. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, FDA released proposed regulations in February 2022 to amend the national standards for licensing of wholesale drug distributors by the states; establish new minimum standards for state licensing third-party logistics providers; and create a federal system for licensure for use in the absence of a State program, each of which is mandated by the DSCSA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be. Regulatory Exclusivity and Approval of Follow- on Products Hatch- Waxman Exclusivity In addition to enacting Section 505 (b) (2) of the FDCA as part of the Hatch- Waxman Amendments to the FDCA, Congress also established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application (ANDA) to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are " abbreviated " because they cannot include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer must rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug (RLD). Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is " bioequivalent " to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if " the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug. " Unlike the 505 (b) (2) NDA pathway that permits a follow- on applicant to conduct and submit data from additional clinical trials or nonclinical studies in order to support the proposed change (s) to the reference product, the ANDA regulatory pathway does not allow applicants to submit new clinical data other than bioavailability or bioequivalence data. Upon approval of an ANDA, the FDA indicates whether the generic product is " therapeutically equivalent " to the RLD in its publication " Approved Drug Products with Therapeutic Equivalence Evaluations, " also referred to as the " Orange Book. " Physicians and pharmacists consider a therapeutically equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA' s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient. Given the importance of such Orange Book designations to the practice of pharmacy, Congress recently directed FDA to perform therapeutic equivalence evaluations for certain 505 (b) (2) drugs no later than six months after approval when the applicant requests such an evaluation. As part of the NDA review and approval process, applicants are required to list with the FDA each patent that has claims that cover the applicant' s product or method of therapeutic use. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential follow- on competitors in support of approval of an ANDA or 505 (b) (2) NDA. FDA' s role in this process is purely " ministerial " and it does not review or assess the claims within each patent to determine whether they cover the drug product or its approved method of use. Patents that may fall outside the scope of what the FDCA and FDA' s implementing regulations define as needing to be listed by the NDA holder are periodically challenged by competitors and other stakeholders, either through FDA' s administrative challenge process or in the court system as anticompetitive or unfair behavior. In particular, the **Federal Trade Commission (** FTC **)** issued a policy statement in September 2023 indicating that it would be scrutinizing the " improper " submission of patents for listing in the Orange Book on the basis that such listings may harm competition from cheaper generic alternatives and keep

brand prices artificially high. The FTC followed that action in November 2023 by publicly calling out over 100 " improper " patent listings made by ten large pharmaceutical companies and initiating an FDA administrative process with respect to those patents. **The controversy regarding the appropriateness of listing such patents has led to numerous lawsuits alleging anticompetitive conduct by biopharmaceutical companies.** It **is unclear** ~~remains to be seen~~ whether the FTC, **under** ~~other~~ -- **the** ~~governmental agencies~~ **Trump Administration** , **will** ~~pharmaceutical manufacturers, or other stakeholders~~ continue to prioritize the policy issue of " improper " patent listings ~~and~~ **or** whether ~~significant litigation will develop in~~ **Congress may take any legislative actions related to** this ~~area~~ **issue** . When an ANDA applicant submits its application to the FDA, it is required to certify to the FDA concerning any patents listed for the reference product in the FDA' s Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505 (b) (2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the NDA- approved product in the Orange Book to the same extent that an ANDA applicant would. If the follow- on applicant does not challenge the innovator' s listed patents, the FDA will not approve the ANDA or 505 (b) (2) application until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product' s listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the follow- on applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505 (b) (2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA or 505 (b) (2) applicant. An ANDA or 505 (b) (2) application also will not be approved until any applicable non- patent exclusivities listed in the Orange Book for the referenced product have expired. The Hatch- Waxman Amendments to the FDCA provided a five- year period of non- patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity (NCE). For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505 (b) (2) NDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of data exclusivity if an NDA or NDA supplement includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. This three- year exclusivity period often protects changes to a previously approved drug product, such as new indications, dosage forms, route of administration or combination of ingredients. Three- year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five- year NCE exclusivity, an award of three- year exclusivity does not block the FDA from accepting ANDAs or 505 (b) (2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; rather, this three- year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving follow- on applications for drugs containing the original active ingredient. Five- year and three- year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505 (b) (1) of the FDCA; however, an applicant submitting a traditional NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well- controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan Drug Designation and Exclusivity Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects either (i) fewer than 200, 000 individuals in the United States, or (ii) more than 200, 000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Legislative proposals to revise or revoke the second option available for a product candidate to receive an orphan designation, the so- called " cost recovery " pathway, are periodically considered by Congress. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use will be disclosed publicly by the FDA; the posting will also indicate whether a drug is no longer designated as an orphan drug. Recent court cases have challenged the FDA' s approach to determining the scope of orphan drug exclusivity; however, at this time the agency continues to apply its long- standing interpretation of the governing regulations and has stated that it does not plan to change any orphan drug implementing regulations. Congress may also act to amend the law in this area at some point in the future. More than one product candidate may receive an orphan drug designation for the same indication, and the same product candidate can be designated for more than one qualified orphan indication. The benefits of orphan drug designation include research and development tax credits and exemption from FDA prescription drug user fees. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process if or when an NDA for the product candidate is filed. If a product that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan product exclusivity, which means that for seven years, the FDA may not approve any other marketing applications for the same drug for the same indication, except under limited circumstances described further below. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different conditions. As a result, the

FDA can still approve different drugs for use in treating the same indication or disease. Additionally, if a drug designated as an orphan product receives marketing approval for an indication broader than what was designated, it may not be entitled to orphan drug exclusivity. Orphan exclusivity will not bar approval of another product with the same drug for the same condition under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety or a major contribution to patient care, or if the company with orphan drug exclusivity cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated. The FDA is now required to publish a summary of the clinical superiority findings when a drug is eligible for orphan product exclusivity on the basis of a demonstration of clinical superiority. In addition, the FDA has finalized guidance indicating that it does not expect to grant any additional orphan drug designation to products for pediatric subpopulations of common diseases. Nevertheless, FDA intends to still grant orphan drug designation to a drug that otherwise meets all other criteria for designation when it prevents, diagnoses or treats either (i) a rare disease that includes a rare pediatric subpopulation, (ii) a pediatric subpopulation that constitutes a valid orphan subset, or (iii) a rare disease that is, in fact, a different disease in the pediatric population as compared to the adult population. Patent Term Extension A patent claiming a prescription drug for which FDA approval is granted may be eligible for a limited patent term extension under the FDCA, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The restoration period granted on a patent covering a new FDA- regulated medical product is typically one- half the time between the date a clinical investigation on human beings is begun and the submission date of an application for premarket approval of the product, plus the time between the submission date of an application for approval of the product and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product' s approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the marketing approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA. Pediatric Exclusivity Pediatric exclusivity is another type of non- patent marketing exclusivity available in the United States and, if granted, it provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity or listed patents. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. Under the Best Pharmaceuticals for Children Act (BPCA), certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA, referred to as a " Written Request, " relating to the use of the active moiety of the product candidate in children. The data do not need to show the product to be effective in the pediatric population studied; rather, the additional protection is granted if the pediatric clinical trial is deemed to have fairly responded to the FDA' s Written Request. Although the FDA may issue a Written Request for studies on either approved or unapproved indications, it may only do so where it determines that information relating to that use of a product candidate in a pediatric population, or part of the pediatric population, may produce health benefits in that population. The issuance of a Written Request does not require the sponsor to undertake the described trials. **Congress periodically considers enacting new incentives or mandates applicable to pediatric drug development, and the regulatory requirements applicable to pediatric drug developers may change in the future. For example, bipartisan legislation introduced in the House of Representatives during the last congressional session (2023- 2024) would have increased funding for pediatric trials; mandated that drugs for rare diseases be studied in children; and granted FDA authority to assess penalties against companies that do not complete required pediatric studies.** Other U. S. Healthcare Laws and Regulations Manufacturing, sales, promotion and other activities following product approval may also be subject to regulation by other regulatory authorities in the United States in addition to the FDA. Depending on the nature of the product, those authorities may include the Centers for Medicare & Medicaid Services (CMS), other divisions of the Department of Health and Human Services (HHS), the DOJ, the ~~Federal Trade Commission (~~FTC ~~)~~, the Drug Enforcement Administration, the Occupational Safety and Health Administration, and state and local governments. For example, in the United States, sales and marketing for prescription biopharmaceutical products must comply with state and federal fraud and abuse laws. These laws include the federal Anti- Kickback Statute **(AKS)** , which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by imprisonment, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, the Patient Protection and Affordable Care Act (ACA), among other things, amended the intent requirement of the federal ~~Anti- Kickback Statute (~~AKS ~~)~~ and two of the five criminal healthcare fraud statutes created by Health Insurance Portability and Accountability Act (HIPAA). A person or entity no longer needs to have actual knowledge of these two provisions in the statute or specific intent to violate them; specifically with respect to the prohibition on executing or attempting to execute a scheme or artifice to defraud or to fraudulently obtain money or property of any healthcare benefit program and the prohibition on disposing of assets to enable a person to become eligible for Medicaid. Moreover, the government may now assert that a claim including items or services resulting from a violation of the federal AKS constitutes a false or fraudulent claim for purposes of the False Claims Act. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U. S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. There also are federal transparency requirements under the Physician Payments

Sunshine Act that require manufacturers of FDA- approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to CMS information related to payments and other transfers of value to physicians, teaching hospitals, and certain advanced non- physician healthcare practitioners and physician ownership and investment interests. Prescription drug products also must meet applicable child- resistant packaging requirements under the U. S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines, or the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act. State, federal, and foreign laws, including the ~~FTCA~~ **Federal Trade Commission Act**, also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Government Regulation Outside the United States In addition to regulations in the United States, we will be subject to a variety of foreign regulations that govern, among other things, clinical trials and any commercial sales and distribution of our products, if approved, either directly or through distribution partners. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries or economic areas, such as the EU, Canada, and the United Kingdom, among other foreign countries, before we may commence clinical trials or market products in those countries or areas. The foreign regulatory approval process includes all of the risks associated with the FDA approval described above, and the time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Some foreign jurisdictions have a drug product approval process similar to that in the United States, which requires the submission of a clinical trial application much like the IND prior to the commencement of clinical studies. In Europe, for example, a ~~clinical trial application (~~ CTA ~~)~~ must be submitted to each country' s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country' s requirements, clinical trial development may proceed. To obtain regulatory approval of a medicinal product candidate under EU regulatory systems, we would be required to submit a Marketing Authorisation Application (MAA), which is similar to the NDA, except that, among other things, there are country- specific document requirements. For countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, and recently the United Kingdom, the requirements governing the conduct of clinical trials, product approval, pricing and reimbursement vary from country to country. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. Moreover, some nations may not accept clinical studies performed for United States approval to support approval in their countries or require that additional studies be performed on natives of their countries. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution. As of January 31, 2020, the United Kingdom is no longer a member state of the EU, and therefore a separate marketing authorization application and approval will be required to market a medicinal product in the United Kingdom. The ~~Medicines and Healthcare products Regulatory Agency (the~~ MHRA ~~)~~ is the United Kingdom' s standalone pharmaceutical regulator. Clinical Trials and Regulation of Medicinal Products in Europe As in the United States, medicinal products can be marketed in the EU only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a EU member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial applications must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents. In April 2014, the new Clinical Trials Regulation, (EU) No 536 / 2014 (Clinical Trials Regulation), was adopted and became effective on January 31, 2022. The Clinical Trials Regulation is directly applicable in all the EU Member States, repealing the prior Clinical Trials Directive 2001 / 20 / EC. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on the duration of the individual clinical trial; if a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial. In addition, use of the new EU- wide application procedure being implemented via the Clinical Trial Information System (CTIS) ~~,~~ became mandatory for new clinical trial application submissions as of February 1, 2023. The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials. To obtain marketing approval of a drug in the EU, an applicant must submit a MAA either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing

authorization by the European Commission that is valid for all EU member states, Iceland, Lichtenstein and Norway. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products (such as gene- therapy, somatic cell-therapy or tissue- engineered medicines) and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of certain diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the European Medicines Agency (EMA) is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use (CHMP). Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop- clocks. The decentralized procedure is available to applicants who wish to market a product in specific EU member states where such product has not received marketing approval in any EU member states before. The decentralized procedure provides for an applicant to apply to one- member state to assess the application (the reference member state) and specifically list other member states in which it wishes to obtain approval (concerned member states). In the EU, only products for which marketing authorizations have been granted may be promoted. A marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re- evaluation of the risk- benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five- year renewal. Any authorization which is not followed by the actual placing of the drug on the **EU** ~~EUmarket~~ -- **market** (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so- called sunset clause). Moreover, even if authorized to be marketed in the EU, prescription medicines may only be promoted to healthcare professionals, not the general public. All promotion should be in accordance with the particulars listed in the summary of product characteristics. Promotional materials must also comply with various laws, and codes of conduct developed by pharmaceutical industry bodies in the EU which govern (among other things) the training of sales staff, promotional claims and their justification, comparative advertising, misleading advertising, endorsements, and (where permitted) advertising to the general public. Failure to comply with these requirements could lead to the imposition of penalties by the competent authorities of the EU member states. The penalties could include warnings, orders to discontinue the promotion of the drug product, seizure of promotional materials, fines and possible imprisonment. In April 2023, the European Commission issued a proposal that will revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the EU. Regulation of New Drugs in the United Kingdom The United Kingdom left the EU on January 31, 2020 (commonly referred to as " Brexit "), with a transitional period that expired on December 31, 2020. The United Kingdom and the EU entered into a trade agreement known as the Trade and Cooperation Agreement, which went into effect on January 1, 2021. We are currently evaluating the potential impacts on our business of the Trade and Cooperation Agreement and guidance issued to date by the United Kingdom' s MHRA regarding the requirements for licensing and marketing medicinal products in the United Kingdom. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of medicinal products is derived from EU Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to such products and the approval of product candidates in the United Kingdom. Such outcomes could make it more difficult and expensive for us to do business in Europe, complicate our clinical, manufacturing and regulatory strategies and impair our ability to obtain and maintain regulatory approval for, and, if approved, commercialize, our products and product candidates in Europe. More recently, in March 2023, the United Kingdom government and the European Commission reached agreement on a regulatory framework to replace the Northern Ireland Protocol, referred to as the Windsor Framework. ~~The~~ **Effective as of January 1, 2025, the** Windsor Framework **introduced new rules for** ~~is expected to apply as of January 1, 2025 and will change the existing system under the Northern Ireland Protocol, including~~ the regulation of pharmaceutical products in the United Kingdom. **The** ~~Specifically, the~~ MHRA ~~will be~~ **is now** responsible for approving all medicines intended to be marketed in the United Kingdom **as a whole** (i. e., Great Britain and Northern Ireland) **. Thus** , ~~while~~ the EMA ~~will~~ **is** no longer ~~be~~ involved in approving medicines intended for sale in Northern Ireland. Regulation of Medicinal Products in Canada Health Canada is the Canadian federal authority that regulates, evaluates and monitors the safety, effectiveness, and quality of drugs and other therapeutic products available to Canadians. Health Canada' s regulatory process for review, approval and regulatory oversight of products is similar to the regulatory process conducted by the FDA. To initiate clinical testing of a product candidate in human subjects in Canada, a CTA must be filed with and approved by Health Canada. In addition, all federally regulated trials must be approved and monitored by research ethics boards. The review boards study and approve study- related documents and monitor trial data. Prior to being given market authorization for a drug product, a manufacturer must present substantive scientific evidence of a product' s safety, efficacy and quality as required by the Food and Drugs Act (Canada) and its associated regulations, including the Food and Drug Regulations. This information is usually submitted in the form of a New Drug Submission (NDS). Health Canada reviews the submitted information, sometimes using external consultants and advisory committees, to evaluate the potential benefits and risks of a drug. If after of the review, the conclusion is that the patient benefits outweigh the risks associated with the drug, the drug is issued a Drug Identification

Number (DIN), followed by a Notice of Compliance (NOC), which permits the market authorization holder (i. e., the NOC and DIN holder) to market the drug in Canada. Drugs granted an NOC may be subject to additional post- market surveillance and reporting requirements. All establishments engaged in the fabrication, packaging / labeling, importation, distribution, and wholesale of drugs and operation of a testing laboratory relating to drugs are required to hold a Drug Establishment License to conduct one or more of the licensed activities unless expressly exempted under the Food and Drug Regulations. The basis for the issuance of a Drug Establishment License is to ensure the facility complies with cGMPs as stipulated in the Food and Drug Regulations and as determined by cGMP inspection conducted by Health Canada. An importer of pharmaceutical products manufactured at foreign sites must also be able to demonstrate that the foreign sites comply with cGMPs, and such foreign sites are included on the importer' s Drug Establishment License. Regulatory obligations and oversight continue following the initial market approval of a pharmaceutical product. For example, every market authorization holder must report any new information received concerning adverse drug reactions, including timely reporting of serious adverse drug reactions that occur in Canada and any serious unexpected adverse drug reactions that occur outside of Canada. The market authorization holder must also notify Health Canada of any new safety and efficacy issues that it becomes aware of after the launch of a product. Pharmaceutical Coverage, Pricing and Reimbursement & Healthcare Reform Sales of our products, if approved for marketing, will depend, in part, on the availability and extent of coverage and reimbursement by third- party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the price and limiting the coverage and reimbursement amounts for medical products and services. There may be significant delays in obtaining coverage and reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. It is time- consuming and expensive to seek reimbursement from third- party payors. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower- cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by third- party payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. In the United States, third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but they also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. Accordingly, one third-party payor' s determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. In addition, the containment of healthcare costs has become a priority for federal and state governments, and the prices of drugs have been a focus in this effort. The U. S. government, state legislatures and foreign governments have shown significant interest in implementing cost- containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost- containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third- party reimbursement for our product candidates or a decision by a third- party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition. Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U. S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmacy benefits managers (PBMs) and other members of the healthcare and pharmaceutical supply chain, an important decision that has led to further and more aggressive efforts by states in this area. The FTC in mid- 2022 also launched sweeping investigations into the practices of the PBM industry **, and published interim reports with its findings in mid- 2024 and January 2025,** that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements **, including in the current 2025- 2026 congressional session** . Indeed both the U. S. Congress and state legislatures are increasingly scrutinizing the industry and proposing novel regulatory approaches to address various perceived public policy concerns. For example, during the ~~current~~ **previous** congressional session, numerous **bipartisan** PBM reforms **were** ~~are being~~ considered in both the Senate and the House of Representatives; they include diverse legislative proposals such as eliminating rebates; divorcing service fees from the price of a drug, discount, or rebate; prohibiting spread pricing; limiting administrative fees; requiring PBMs to report formulary placement rationale; promoting transparency. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including biopharmaceutical product developers like us. Further, in August 2022, President Biden signed into the law the Inflation Reduction Act of 2022 (the IRA). Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. A manufacturer of drugs covered by Medicare Parts B or D must now pay a rebate to the federal government if their drug product' s price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by

Medicare Parts B or D. Additionally, starting for payment year 2026, CMS ~~will~~ **is** ~~negotiate~~ **negotiating** drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities **entering** ~~and entered~~ into agreements to conduct price negotiations with pharmaceutical manufacturers in October 2023 **and ultimately announcing the first round of negotiated prices for the first 10 drugs in August 2024; those negotiated " maximum fair prices " will be effective as of January 1, 2026 (payment year 2026). CMS is currently engaged in its second round of negotiations and published the next 15 drugs selected for negotiation in January 2025** . However, the impact of this program on the biopharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e. g., the U. S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. ~~Those~~ -- **The outcome of such ongoing** lawsuits ~~are currently ongoing~~ **, as well as potential legislative changes enacted by Congress or programmatic changes implemented at CMS by the Trump Administration, may impact the IRA drug price negotiation program in the future** . In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the EU, the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89 / 105 / EEC (the Price Transparency Directive). The aim of the Price Transparency Directive is to ensure that pricing and reimbursement mechanisms established in the EU Member States are transparent and objective, do not hinder the free movement of and trade in medicinal products in the EU, and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in the individual EU Member States, nor does it have any direct consequence for pricing or reimbursement levels in the individual EU Member States. The EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices and / or reimbursement levels of medicinal products for human use. A EU Member State may approve a specific price or level of reimbursement for the medicinal product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the medicinal product on the market, including volume- based arrangements, caps and reference pricing mechanisms. Health Technology Assessment (HTA) of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including France, Germany, Ireland, Italy and Sweden. The HTA process in the EU Member States is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact, and the economic and societal impact of the use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost- effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product vary between the EU Member States. For example, EU Member States that have not yet developed HTA mechanisms could rely to some extent on the HTA performed in countries with a developed HTA framework when adopting decisions concerning the pricing and reimbursement of a specific medicinal product. Separately from cost containment efforts, in the United States and some foreign jurisdictions, there also have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates or restrict or regulate post-approval activities. For example, in April 2023 the European Commission issued a proposal for anew Directive and a new Regulation, which will revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the EU. The FDA' s and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our current or future product candidates. Data Privacy and the Protection of Personal Information We are subject to laws and regulations governing data privacy and the protection of personal information including health information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which will continue to affect our business. In the United States, we may be subject to state security breach notification laws, state laws protecting the privacy of health and personal information and federal and state consumer protections laws that regulate the collection, use, disclosure and transmission of personal information. These laws overlap and often conflict **,** and each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. If we fail to comply with applicable laws and regulations, we could be subject to penalties or sanctions, including criminal penalties. Our customers and research partners must comply with laws governing the privacy and security of health information, including HIPAA and state health information privacy laws. If we knowingly obtain health information that is protected under HIPAA, called " protected health information, " our customers or research collaborators may be subject to enforcement, and we may have direct liability for the unlawful receipt of protected health information or for aiding and abetting a HIPAA violation. **In addition** ~~State laws protecting health and personal information are becoming increasingly stringent. For example~~ , the California Confidentiality of Medical Information Act imposes restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. **Other federal and state laws establish additional requirements for protecting the privacy and security of health information that is not protected by HIPAA. For instance, Washington state recently passed the " My Health My Data " Act, which will regulate " consumer health data, " which is defined as " personal information that is linked or**

reasonably linkable to a consumer and that identifies a consumer' s past, present, or future physical or mental health. " The **" My Health My Data " Act provides exemptions for personal data used or shared in connection with certain research activities, including data subject to 45 C. F. R. Parts 46, 50 and 56. Notably, the " My Health My Data " Act contains a private right of action. In addition, Nevada recently enacted a consumer health data privacy bill, SB 370, which also regulates " consumer health data " and shares many similarities with Washington' s " My Health My Data " Act, and Connecticut recently amended its comprehensive privacy law to include heightened regulation of " consumer health data. " Additional states may adopt health- specific privacy laws that could impact our business activities and our collection and handling of health- related data. More broadly, various state laws regulate the processing of personal information. For example, California has enacted the** California Consumer Privacy Act (CCPA) ~~mirrors~~ **, which went into effect in January of 2020. The CCPA gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that may increase data breach litigation. Although the CCPA includes exemptions for certain categories of health information, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. Additionally in 2020, California voters passed the California Privacy Rights Act (CPRA), which went into full effect on January 1, 2023. The CPRA significantly amended the CCPA, potentially resulting in further uncertainty, additional costs and expenses in an effort to comply and additional potential for harm and liability for failure to comply. Among other things, the CPRA established a new regulatory authority, the California Privacy Protection Agency, which is tasked with enacting new regulations under the CPRA and has expanded enforcement authority. In addition to California, more U. S. states are enacting similar legislation, increasing compliance complexity and increasing risks of failures to comply. In 2023, comprehensive privacy laws in Virginia, Colorado, Connecticut, and Utah all took effect, and laws in Montana, Oregon, and Texas took effect during 2024. Laws in** a number of ~~the~~ **other** ~~key provisions~~ **US states took effect, or are set to take effect, in 2025, in 2026, and beyond. Additional U. S. states have proposals under consideration, all** of **which are likely to increase our regulatory compliance costs and risks, exposure to regulatory enforcement action, and other liabilities. Numerous other countries have, or are developing, laws governing the collection, use and transmission of personal information as well. For example, the European Parliament and the Council of the European Union adopted a comprehensive general data privacy framework called** the General Data Protection Regulation (GDPR) **which** ~~described below. The CCPA establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. The California Consumer Rights Act (CPRA) became effective on January 1, 2023, strengthening elements of the CCPA. Since passage of the CCPA, several other states (e. g., Connecticut, Colorado, Virginia, Delaware, Florida, Iowa, Montana, Oregon, Tennessee, Texas and Utah) have also enacted comprehensive consumer privacy laws that include key differences from California' s law, further complicating compliance by industry and other stakeholders. Other states in the United States are considering privacy laws similar to the CCPA. In Europe, the GDPR~~ went into effect in May 2018, **and** ~~implementing~~ **implemented** a broad data protection framework that expanded the scope of EU data protection law, ~~including~~ **and applies** to ~~non-~~ **entities located inside and outside of the** EU ~~entities~~ that process, or control the processing of, personal data relating to individuals located in the EU, including clinical trial data. The GDPR ~~sets out a number of~~ **, which is wide- ranging in scope, imposes several** requirements ~~that must be complied with when handling~~ **relating to the consent of the individuals to whom** the personal data **relates,** ~~of EU- based data subjects including: providing expanded disclosures about how their~~ -- **the information provided to the individuals, the security and confidentiality of the** personal data ~~will be used; higher standards for organizations to demonstrate that they have obtained valid consent or have another legal basis in place to justify their data processing activities; the obligation to appoint data protection officers in certain circumstances; new rights for individuals to be " forgotten " and rights to data portability~~ , ~~as well as enhanced current rights (e. g. access requests); the principal of accountability and demonstrating compliance through policies, procedures, training and audit; and a new mandatory~~ data breach ~~regime~~ **notification, and the use of third- party processors in connection with the processing of the personal data** . In particular, medical or health data, **and** genetic ~~data~~ and biometric data ~~where the latter is~~ used to uniquely identify an individual are all classified as " special category " data under the GDPR and ~~afforded greater protection~~ **are subject to heightened restrictions** and ~~require additional~~ compliance obligations. Further, EU member states have a broad right to impose additional conditions – including restrictions – on these data categories. This is because the GDPR allows EU member states to derogate from the requirements of the GDPR mainly in regard to specific processing situations (including special category data and processing for scientific or statistical purposes). As ~~the~~ EU **member** states continue to reframe their national legislation to harmonize with the GDPR, we will need to monitor compliance with all relevant EU member states' laws and regulations, including where permitted derogations from the GDPR are introduced ~~. The GDPR also prohibits the international transfer of personal data from the EU to countries outside of the EU unless made to a country deemed to have adequate data privacy laws by the European Commission or made through an approved data transfer mechanism. On July 16, 2020, the Court of Justice of the European Union (CJEU), issued a landmark opinion in the case Maximilian Schrems vs. Facebook (Case C- 311 / 18), called Schrems II. This decision (a) calls into question commonly relied upon data transfer mechanisms as between the EU Member States and the United States (such as the Standard Contractual Clauses) and (b) invalidates the EU- U. S. Privacy Shield on which many companies had relied as an acceptable mechanism for transferring such data from the EU to the United States. On July 10, 2023, the European Commission adopted an adequacy decision for a new mechanism for transferring data from the EU to the United States – the EU- US Data Privacy Framework~~

~~(the Framework). The Framework provides individuals in the EU with several new rights, including the right to obtain access to their data, or obtain correction or deletion of incorrect or unlawfully handled data. The adequacy decision followed the signing of an executive order introducing new binding safeguards to address the points raised in the Schrems II decision. Notably, the new obligations were geared to ensure that data can be accessed by US intelligence agencies only to the extent necessary and proportionate and to establish an independent and impartial redress mechanism to handle complaints from Europeans concerning the collection of their data for national security purposes. The European Commission will continually review developments in the United States along with its adequacy decision. Adequacy decisions can be adapted or even withdrawn in the event of developments affecting the level of protection in the applicable jurisdiction. Future actions of EU data protection authorities are difficult to predict. Some customers or other service providers may respond to these evolving laws and regulations by asking us to make certain privacy or data- related contractual commitments that we are unable or unwilling to make. This could lead to the loss of current or prospective customers or other business relationships~~ . Relatedly, following Brexit and the expiry of the Brexit transition period, which ended on December 31, 2020, the EU GDPR has been implemented in the United Kingdom (as the UK GDPR). The UK GDPR sits alongside the United Kingdom Data Protection Act 2018 which implements certain derogations in the EU GDPR into United Kingdom law. Under the UK GDPR, companies not established in the United Kingdom but who process personal data in relation to the offering of goods or services to individuals in the United Kingdom, or to monitor their behavior will be subject to the UK GDPR – the requirements of which are (at this time) largely aligned with those under the GDPR and as such, may lead to similar compliance and operational costs with potential fines of up to £ 17. 5 million or 4 % of global turnover. **Transfers of personal data to certain countries outside of the EU and the UK are also highly regulated under the GDPR and UK GDPR. For example, the GDPR only permits exports of personal data outside of the EU to " non- adequate " countries where there is a suitable data transfer mechanism in place to safeguard personal data (e. g., the EU Commission approved Standard Contractual Clauses or certification under the newly- adopted Data Privacy Framework). On July 16, 2020, the Court of Justice of the EU (CJEU), issued a landmark opinion in the case Maximilian Schrems vs. Facebook (Case C- 311 / 18) (Schrems II). This decision calls into question certain data transfer mechanisms as between the EU member states and the U. S. The CJEU is the highest court in Europe and the Schrems II decision heightened the burden to assess U. S. national security laws on their business, and future actions of EU data protection authorities are difficult to predict at this time. While the Data Privacy Framework was meant to address the concerns raised by the CJEU in Schrems II, it will likely be subject to future legal challenges. Consequently, there is some risk of any data transfers from the EU being halted. If we have to rely on third parties to carry out services for us, including processing personal data on our behalf, we are required under GDPR to enter into contractual arrangements to flow down or help ensure that these third parties only process such data according to our instructions and have sufficient security measures in place. Any security breach or non- compliance with our contractual terms or breach of applicable law by such third parties could result in enforcement actions, litigation, fines and penalties or adverse publicity and could cause customers to lose trust in us, which would have an adverse impact on our reputation and business. Any contractual arrangements requiring the processing of personal data from the EU to us in the U. S. will require greater scrutiny and assessments as required under Schrems II and may have an adverse impact on cross- border transfers of personal data or increase costs of compliance. Applicable data privacy and data protection laws may conflict with each other, and by complying with the laws or regulations of one jurisdiction, we may find that we are violating the laws or regulations of another jurisdiction. Despite our efforts, we may not have fully complied in the past and may not in the future. That could require us to incur significant expenses, which could significantly affect our business. Failure to comply with data protection laws may expose us to risk of enforcement actions taken by data protection authorities or other regulatory agencies, private rights of action in some jurisdictions, and potential significant penalties if we are found to be non- compliant. Furthermore, the number of government investigations related to data security incidents and privacy violations continue to increase and government investigations typically require significant resources and generate negative publicity, which could harm our business and reputation.** United States Foreign Corrupt Practices Act In general, the Foreign Corrupt Practices Act of 1977, as amended (FCPA), prohibits offering to pay, paying, promising to pay, or authorizing the payment of money or anything of value to a foreign official in order to influence any act or decision of the foreign official in his or her official capacity or to secure any other improper advantage in order to obtain or retain business for or with, or in order to direct business to, any person. The prohibitions apply not only to payments made to " any foreign official, " but also those made to " any foreign political party or official thereof, " to " any candidate for foreign political office " or to any person, while knowing that all or a portion of the payment will be offered, given, or promised to anyone in any of the foregoing categories. " Foreign officials " under the FCPA include officers or employees of a department, agency, or instrumentality of a foreign government. The term " instrumentality " is broad and can include state- owned or state- controlled entities. Importantly, United States authorities deem most healthcare professionals and other employees of foreign hospitals, clinics, research facilities and medical schools in countries with public healthcare and / or public education systems to be " foreign officials " under the FCPA. When we interact with foreign healthcare professionals and researchers in testing and marketing our products abroad, should any of our product candidates receive foreign regulatory approval in the future, we must have policies and procedures in place sufficient to prevent us and agents acting on our behalf from providing any bribe, gift or gratuity, including excessive or lavish meals, travel or entertainment in connection with marketing our products and services or securing required permits and approvals. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Environmental, Health and Safety Regulation We are subject to numerous federal, state and local environmental, health and safety (EHS) laws and regulations relating to, among other matters, safe working

conditions, product stewardship, environmental protection, and handling or disposition of products, including those governing the generation, storage, handling, use, transportation, release, and disposal of hazardous or potentially hazardous materials, medical waste, and infectious materials that may be handled by our partner research laboratories. Some of these laws and regulations also require us to obtain licenses or permits to conduct our operations. If we fail to comply with such laws or obtain and comply with the applicable permits, we could face substantial fines or possible revocation of our permits or limitations on our ability to conduct our operations. Certain of our development and manufacturing activities may involve, from time to time, use of hazardous materials, and we believe we are in compliance with the applicable environmental laws, regulations, permits, and licenses. However, we cannot ensure that EHS liabilities will not develop in the future. EHS laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits. Human Capital Resources As of March ~~1~~ **7** , ~~2024~~ **2025 we** ~~,~~ ~~GRI~~ had ~~4~~ **four** employees **,** of which ~~all~~ **three** were full- time employees **and one was part- time** . We believe the intellectual capital of our current and future employees and consultants is an impactful driver of our business and is key to our future prospects. GRI' s Corporate Information Vallon Pharmaceuticals, Inc. (Vallon) was incorporated under the laws of the State of Delaware in January 2018, and completed its organization, formation and initial capitalization activities effective in June 2018. GRI Bio Operations, Inc. (GRI Operations), formerly known as GRI Bio, Inc., was incorporated under the laws of the State of Delaware in May 2009 under the name Glycoregimmune, Inc., and amended its certificate of incorporation to change its name to GRI Bio, Inc. on July 29, 2015. On April 21, 2023, pursuant to that Agreement and Plan of Merger, dated as of December 13, 2022, as amended on February 17, 2023 (the Merger Agreement), by and among Vallon, GRI Operations and Vallon Merger Sub, Inc., a Delaware corporation and wholly owned subsidiary of the Company (Merger Sub), Merger Sub was merged with and into GRI (the Merger), with GRI surviving the Merger as a wholly owned subsidiary of the Company. In ~~connection with the Merger, and prior to the effective time of the Merger (the Effective Time), the Company effected a reverse stock split of the Company' s common stock at a ratio of 1- for- 30 (the April Reverse Split). Also, in~~ connection with the closing of the Merger (the Closing), the Company amended its certificate of incorporation and bylaws to change its name from " Vallon Pharmaceuticals, Inc. " to " GRI Bio, Inc. " Our principal executive offices are located at 2223 Avenida De La Playa # 208, La Jolla, CA 92037. Available Information We file our annual reports on Form 10- K, quarterly reports on Form 10- Q and current reports on Form 8- K, proxy and information statements, and other information with the SEC under the Securities Exchange Act of 1934, as amended (the Exchange Act). You can read our SEC filings at the SEC' s website. The SEC maintains an internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at http: / / www. sec. gov. Our website address is www. gribio. com. The information contained in, and that can be accessed through, our website is not incorporated into and is not part of this Annual Report. Emerging Growth Company Status We are an " emerging growth company, " as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act) and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not applicable to emerging growth companies. These exemptions include: • reduced disclosure about our executive compensation arrangements; • no non- binding stockholder advisory votes on executive compensation or golden parachute arrangements; and • exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting. We have taken advantage of reduced reporting requirements in this report and may continue to do so until such time that we are no longer an emerging growth company. We will remain an " emerging growth company " until the earliest of (a) the last day of the fiscal year in which we have total annual gross revenues of $ 1. 235 billion or more, (b) December 31, 2026, the last day of the fiscal year following the fifth anniversary of the completion of the IPO, (c) the date on which we have issued more than $ 1. 0 billion in nonconvertible debt during the previous three years or (d) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period for complying with new or revised accounting standards. Item 1A. RISK FACTORS ~~You~~ **Careful consideration** should ~~consider carefully~~ **be given to** the following ~~risks~~ **risk factors** ~~described below~~ , ~~together with~~ **in addition to** the other information contained in this Annual Report and in our other public filings, in evaluating our **company and** business **. Investing in our securities involves a high degree of risk** . If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected **and** ~~. In these~~ -- **the trading** ~~circumstances, the market~~ price of our **securities** ~~common stock would~~ **could** ~~likely~~ decline **. Our actual results could differ materially from those anticipated in the forward looking statements as a result of factors that are described below and elsewhere in this Annual Report** . We have incurred significant net losses since our inception and have financed our operations principally through equity and debt financing. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss was $ **8. 2 million and $** 13. 0 ~~million and $ 3. 2~~ million for the years ended December 31, **2024 and** 2023 ~~and 2022~~ , respectively. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~31~~ **39** . ~~5~~ **7** million. We have devoted substantially all of our resources and efforts to research and development, and we expect that it will be several years, if ever, before we generate revenue from product sales. Even if we receive marketing approval for and commercialize one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to develop and, if approved, market additional potential product candidates. We expect to continue to incur significant losses for the foreseeable future, and we anticipate that our expenses will increase substantially if, and as, we: • advance our lead product candidate, GRI- 0621, and our other product candidates through clinical development, and, if successful, later- stage clinical trials; • discover and develop new product candidates; • advance our preclinical development programs into clinical development; • further develop

manufacturing processes and manufacture our product candidates; • experience delays or interruptions to preclinical studies, clinical trials, our receipt of services from our third- party service providers on whom we rely, or our supply chain due to pandemics, supply chain and labor shortages, labor strikes, work stoppages or boycotts, natural disasters and geopolitical conflicts, such as the conflicts in Ukraine and the Middle East; • seek regulatory approvals for any product candidates that successfully complete clinical trials; • commercialize GRI- 0621, our other product candidates and any future product candidates, if approved; • increase the amount of research and development activities to identify and develop product candidates; • hire additional clinical development, quality control, scientific and management personnel; • expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development and manufacturing efforts and our operations as a public company; • establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any products for which we may obtain marketing approval and intend to commercialize on our own or jointly with third parties; • maintain, expand and protect our intellectual property portfolio; • invest in or in- license other technologies or product candidates; ~~• we are, as described further below, unable to comply with the obligations of our registration rights agreements;~~ and • continue to build out our organization to engage in such activities. To become and remain profitable, we must develop and eventually commercialize products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials, obtaining marketing approval for product candidates, manufacturing, marketing, and selling products for which we may obtain marketing approval and satisfying any post- marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. Developing biotechnology and biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time- consuming, expensive, and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our planned clinical trials of GRI- 0621, GRI- 0803 and any other product candidates that we may develop or seek regulatory approvals for and, if approved, launch and commercialize. In particular, we do not expect to be able to continue our clinical trials or development efforts without raising additional funds. We also expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to maintain our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce, or eliminate one or more of our research and drug development programs or future commercialization efforts. As of December 31, ~~2023~~ **2024**, we had approximately $ ~~1~~ **5**. ~~8~~ **0** million in cash and cash equivalents and an accumulated deficit of approximately $ ~~31~~ **39**. ~~5~~ **7** million. If we secure additional funds, we expect to devote substantial financial resources to our planned activities, particularly as we conduct our clinical trials of GRI- 0621 and GRI- 0803, advance our discovery programs and continue our product development efforts. ~~We are also party to a registration rights agreement that requires us to, among other things, obtain effectiveness of a registration statement and to maintain the effectiveness of the registration statements for resale of the shares underlying the Exchange Warrants (as defined below) and the Equity Warrants (as defined below). If we fail to comply with these obligations, we would be subject to substantial cash penalties and, as of the date of this Annual Report, would likely not have the resources to make such payments and continue our operations. On October 13, 2023, we filed a registration statement on Form S- 3 for the offer and resale of the shares underlying the Exchange Warrants and the Equity Warrants, as amended by a Pre- Effective Amendment No. 1 to Form S- 3 on Form S- 1, filed on December 4, 2023, which was declared effective on December 15, 2023.. On February 1, 2024, we entered into a securities purchase agreement (the Purchase Agreement) with each purchaser identified on the signature pages thereto, pursuant to which we agreed to issue and sell, in a public offering, (i) 330, 450 shares (the Shares) of Common Stock, (ii) 4, 669, 550 pre- funded warrants (the Pre- Funded Warrants) exercisable for an aggregate of 4, 669, 550 shares of Common Stock, (iii) 5, 000, 000 Series B- 1 common warrants (the Series B- 1 Common Warrants) exercisable for an aggregate of 5, 000, 000 shares of Common Stock, and (iv) 5, 000, 000 Series B- 2 common warrants (the Series B- 2 Common Warrants, and together with the Series B- 1 Common Warrants, the Common Warrants) exercisable for an aggregate of 5, 000, 000 shares of Common Stock. The Common Warrants together with the Pre- Funded Warrants are referred to in this Annual Report as the " Warrants. " The securities were offered in combinations of (a) one Share or one Pre- Funded Warrant, together with (b) one Series B- 1 Common Warrant and one Series B- 2 Common Warrant, for a combined purchase price of $ 1. 10 (less $ 0. 0001 for each Pre- Funded Warrant). In addition, we expect to continue to incur additional costs associated with operating as a public company.~~ Based on our current operating plan, we believe that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements ~~only~~ into the second ~~half~~ **quarter** of ~~2024~~ **2025**. ~~The Series T Warrants issued pursuant to that certain Securities Purchase Agreement, dated December 13, 2022, by and among the Company, GRI Operations and Altium Growth Fund L. P. (Altium), currently can be force exercised~~. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. Our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and we will require additional funding to recommence development of our product candidates. Our spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development, and assuming approval, marketing and commercialization activities. We will need to raise ~~substantial~~ **additional** funds in the near term in ~~addition to the funds raised in the offering completed in February 2024 in~~ order to ~~regain~~ **maintain** compliance with Nasdaq' s **continued listing** ~~currently applicable stockholders' equity requirement~~ **requirements** and continue operations ~~, as discussed further below. We intend to~~

~~raise additional funds in the near term~~ . However, additional funding may not be available on acceptable terms, if at all. Until we can generate sufficient revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Further, to the extent that we raise additional capital through the sale of Common Stock or securities convertible or exchangeable into Common Stock, our stockholders' ownership interest will be diluted. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional capital through marketing and distribution arrangements or collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish certain valuable intellectual property or other rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also may be required to seek collaborators for any of our product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. Market volatility resulting from inflation, pandemics, geopolitical events or other financial markets factors could also adversely impact our ability to access capital as and when needed. If we are unable to secure adequate additional funding, we will need to reevaluate our operating plans and may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, delay, scale back or eliminate some or all of our development programs, relinquish rights to our technology on less favorable terms than we would otherwise choose or cease operations entirely. These actions could materially impact our business, results of operations, our future prospects and the value of shares of our Common Stock, and as a result, our stockholders may receive no value for their investment. In addition, attempting to secure additional financing diverts the time and attention of management from day- to- day activities and distract from our discovery and product development efforts. We have incurred losses since inception and, to date, have financed our operations by issuing equity and debt securities. We anticipate that we will continue to incur losses and generate negative operating cash flows in the foreseeable future as we continue to develop our drug candidates and that we will require additional funding to support our planned operating activities. The report of our independent registered public accounting firm on our financial statements as of and for the year ended December 31, ~~2023~~ **2024** includes an explanatory paragraph indicating that there is substantial doubt about our ability to continue as a going concern. Until such time, if ever, in which we can generate substantial product revenue, we expect we may continue to fund our operations and capital funding needs through equity offerings, debt financings or other capital sources, including strategic licensing, collaboration or other similar agreements. As stated above, if we are unable to secure adequate additional funding, we will need to reevaluate our operating plans and may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, delay, scale back or eliminate some or all of our development programs, or relinquish rights to our technology on less favorable terms than it would otherwise choose. These actions could materially impact our business, results of operations, our future prospects and the value of shares of our Common Stock, and, as a result, our stockholders may receive no value for their investment. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. Because GRI- 0621 is our lead product candidate, if GRI- 0621 encounters safety or efficacy problems, **additional** development delays, regulatory issues or other problems, our development plans and business would be significantly harmed. Before we can generate any revenue from sales of our lead product candidate, GRI- 0621, GRI- 0803 or any of our other product candidates, we must undergo additional clinical development, regulatory review, and approval in one or more jurisdictions. These efforts will require substantial investment, and we may not have the financial resources to continue development of our product candidates. We may experience setbacks that could delay or prevent regulatory approval of, or the extent of regulatory protection or our ability to commercialize, our product candidates, including: • negative or inconclusive results from our preclinical studies or clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program; • product- related side effects experienced by subjects in our clinical trials or by individuals using drugs or therapeutics similar to our product candidates; • **further** delays in submitting INDs or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced; • conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials, including any regulatory requirements for certain outcomes be measured during product development or to support market authorization; • delays in enrolling subjects in clinical trials, including due to pandemics, labor shortages or other geopolitical events; • high drop- out rates of subjects from clinical trials; • inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials; • challenges manufacturing our product candidates to regulatory requirements in a cost effective manner; • greater than anticipated clinical trial costs; • inability to compete with other therapies; • failure to secure or maintain orphan designation in some jurisdictions; • poor efficacy of our product candidates during clinical trials; • unfavorable FDA or other regulatory agency inspection and review of a clinical trial site; • failure of our third- party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all; • delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or • varying interpretations of data by the FDA and similar foreign regulatory agencies. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and our manufacturing, marketing, distribution and sales efforts or that of any future collaborator. Delays in regulatory approvals or our failure to obtain regulatory approvals would harm our business, prospects and results of operations. To obtain the requisite regulatory approvals to commercialize any product

candidates, we must demonstrate through extensive ~~preclinical~~ **nonclinical** studies and clinical trials that our product candidates are safe and effective in humans for their intended use (s). Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, the general approach for FDA approval of a new drug is dispositive data from two well- controlled, Phase 3 clinical trials of the relevant drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A product candidate can fail at any stage of testing, even after observing promising signals of activity in earlier preclinical studies or clinical trials. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. In general, most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our ~~future~~ clinical trials will ultimately be successful or support further clinical development of GRI- 0621, GRI- 0803 or any of our other product candidates. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including: • preclinical studies or clinical trials may show the product candidates to be less effective than expected (e. g., a clinical trial could fail to meet its primary endpoint (s)) or to have unacceptable side effects or toxicities; • failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful; • development of competing products in the same disease state; • manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that make a product candidate uneconomical; and • the proprietary rights of others and their competing products and technologies that may prevent one of our product candidates from being commercialized. **In 2022,** Congress ~~also recently~~ amended the FDCA to require sponsors of a Phase 3 clinical trial, or other " pivotal study " of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must describe appropriate diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Although none of our product candidates has reached Phase 3 of clinical development, we must submit a diversity action plan to the FDA by the time we submit a Phase 3 trial, or pivotal study, protocol to the agency for review, unless we are able to obtain a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect the planning and timing of any future Phase 3 trial for our product candidates ~~or what specific information FDA will expect in such plans~~. However, initiation of such trials may be delayed if the FDA objects to our proposed diversity action plans for any future Phase 3 trial for our product candidates, and we may experience difficulties recruiting a diverse population of patients in attempting to fulfill the requirements of any approved diversity action plan. In addition, the standards that the FDA and comparable foreign regulatory authorities use when regulating our product candidates require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations. Examples of such regulations include future legislation or administrative action, or changes in FDA policy during the period of product development and FDA regulatory review. We cannot predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. For example, in April 2023 the European Commission issued a proposal for a new directive and a new regulation, which will revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the EU. The FDA may also require a panel of experts, referred to as an advisory committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the advisory committee, although not binding on the FDA, may have a significant impact on the agency' s decision- making process and our ability to obtain approval of any product candidates that we develop. If we seek to conduct clinical trials in foreign countries or pursue marketing approvals in foreign jurisdictions, we must comply with numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third- party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the United States and vice versa. Our competitors also may obtain FDA or regulatory approval from comparable foreign regulatory authorities for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. If we encounter **additional** difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of completion of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical trials if we **again** encounter difficulties in enrollment. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion **. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons** . The enrollment of patients

depends on many factors, including: • the patient eligibility and exclusion criteria defined in the protocol; • the size of the patient population required for analysis of the trial' s primary endpoints and the process for identifying patients; • the willingness or availability of patients to participate in our trials; • the proximity of patients to trial sites; • the design of the trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating; • the availability of competing commercially available therapies and other competing product candidates' clinical trials; • our ability to obtain and maintain patient informed consents; **• our ability to establish new sites in accordance with applicable regulatory requirements;** and • the risk that patients enrolled in clinical trials will drop out of the trials before completion. For example, when we evaluated GRI- 0621 in a pilot Phase 2a trial in hepatically impaired chronic liver disease patients, the study was originally intended to evaluate 60 patients but due to recruitment challenges and updated guidance from the FDA regarding the design of NASH clinical studies we made the administrative decision to halt the study after enrolling 14 patients. ~~Additionally~~ **In addition, we previously expected topline results from our Phase 2a trial for GRI- 0621 to be available in the fourth quarter of 2024 and this has since been delayed to the third quarter of 2025 primarily as a result of delayed enrollment. Enrollment in this trial continues to be somewhat unpredictable. Further**, we are initially developing GRI- 0621 for the treatment of IPF, which is an orphan indication. As a result, we **have and** may **again** encounter difficulties enrolling subjects in our clinical trials of GRI- 0621 due, in part, to the small size of this patient population or the burden of safety labs included in the clinical protocol ~~, among other things~~. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition may reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Further, timely enrollment in clinical trials is reliant on clinical trial sites which may be adversely affected by global health matters, including, among other things, pandemics, supply and labor shortages and geopolitical events. These delays and potential delays to development timelines may adversely affect our business, prospects and results of operations. Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we publicly disclose interim, preliminary or topline data from our clinical studies, which is based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analysis of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline or preliminary results of clinical trials we report may differ from final results reported for those studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final, complete data are available. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. There can be no guarantee that a favorable interim analysis will result in a favorable final result at the completion of the clinical trial. Likewise, in light of the fact that our evaluation of GRI- 0621 in a pilot Phase 2a trial in hepatically impaired chronic liver disease patients was originally intended to evaluate 60 patients and that we made the administrative decision to halt the study after enrolling 14 patients due to recruitment challenges and updated guidance from the FDA regarding the design of NASH clinical studies, our disclosure that GRI- 0621 was observed to be well - tolerated and showed improvements in liver function tests, serum CK- 18, and in iNKT cell activity in this limited number of patients is qualified by the fact that the study was underpowered to meet its endpoints with statistical significance. Our observations from this pilot Phase 2a trial may not be indicative of results from any potential future ~~pre- clinical~~ **preclinical** studies or clinical trials. Changes in regulatory requirements, FDA guidance or unanticipated events during our preclinical studies and clinical studies of our product candidates may occur, which may result in changes to preclinical or clinical study protocols or additional preclinical or clinical study requirements, which could result in increased costs to us and could delay our development timeline. Changes in regulatory requirements, FDA guidance or unanticipated events during our preclinical studies and clinical studies may force us to amend preclinical studies and clinical study protocols. The FDA or comparable foreign regulatory authorities may also impose additional preclinical studies and clinical study requirements. Amendments or changes to our clinical study protocols, including changes to endpoints, would require resubmission to the FDA or comparable foreign regulatory authorities and IRBs for review and approval, which may increase the cost or delay the timing or successful completion of clinical studies. Similarly, amendments to our preclinical studies may increase the cost or delay the timing or successful completion of those preclinical studies. If we experience delays completing, or if we terminate, any of our preclinical or clinical studies, or if we are required to conduct additional preclinical or clinical studies, the commercial prospects for our product candidates may be harmed and our ability to recognize product revenue will be delayed. If product liability lawsuits are brought against us, we may incur substantial financial or other liabilities and may be required to limit commercialization of our product candidates. We face an inherent risk of product liability as a result of testing GRI- 0621, GRI- 0803 and any of our other product candidates in clinical trials and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. As an oral formulation of an active ingredient that has previously been approved by

FDA only for topical administration, in particular, GRI- 0621 may be subject to the identification of new serious adverse events as it is administered to larger numbers of research subjects in order to evaluate its safety / effectiveness in chronic use indications and in new patient populations. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense of these claims would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • inability to bring a product candidate to the market; • decreased demand for our products; • injury to our reputation; • withdrawal of clinical trial participants and inability to continue clinical trials; • initiation of investigations by regulators; • fines, injunctions or criminal penalties; • costs to defend the related litigation; • diversion of management' s time and our resources; • substantial monetary awards to trial participants; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • exhaustion of any available insurance and our capital resources; • the inability to commercialize any product candidate, if approved; and • decline in our share price. 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 products we develop. We may be unable to obtain, or may obtain on unfavorable terms, clinical trial insurance in amounts adequate to cover any liabilities from any of our clinical trials. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise. We expect to utilize the FDA' s Section 505 (b) (2) pathway for our lead product candidate, and if that pathway is not available, the development of our product candidate will likely take significantly longer, cost significantly more and entail significantly greater complexity and risk than currently anticipated, and, in any case, may not be successful. We intend to develop and seek approval for GRI- 0621, and potentially other candidates that we may develop, pursuant to the FDA' s 505 (b) (2) pathway. If the FDA determines that we may not use this regulatory pathway, then we would need to seek regulatory approval via a " full " or " stand- alone " NDA under Section 505 (b) (1) of the FDCA. This would require us to conduct additional clinical trials, provide additional safety and efficacy data and other information, and meet additional standards for regulatory approval including possibly nonclinical data. If this were to occur, the time and financial resources required to obtain FDA approval, as well as the development complexity and risk associated with these programs, would likely substantially increase, which could have a material adverse effect on our business and financial condition. The Drug Price Competition and Patent Term Restoration Act of 1984, informally known as the Hatch-Waxman Act, added Section 505 (b) (2) to the FDCA. Section 505 (b) (2) permits the filing of an NDA where at least some of the information required for approval comes from studies and information that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505 (b) (2), if applicable to ~~us~~ **certain of our product candidates** under the FDCA **,** ~~. This~~ would allow an NDA we submit to the FDA to rely in part on data in the public domain or the FDA' s prior conclusions regarding the safety and effectiveness of approved compounds ~~, which~~ **. Such an approach** could expedite the development programs for GRI- 0621. In addition, although 505 (b) (2) applicants have significant flexibility in the types of studies, data, and information they may submit in a 505 (b) (2) NDA to support the requirements for NDA approval, establish a favorable benefit- risk profile for the new drug product, and demonstrate the new drug' s substantial evidence of effectiveness for its proposed intended use (s), the applicant bears the burden of establishing a scientific bridge between its drug product and each listed drug that the applicant seeks to rely upon and that the studies it is proposing to conduct are scientifically justified. If the FDA disagrees with the applicant' s proposed development plan for the follow- on drug product, it may require ~~companies~~ **the sponsor** to perform additional studies or measurements, including nonclinical and clinical studies, to support the change from the approved product. FDA also may request or require studies to incorporate additional clinical endpoints than what the sponsor proposes. The extent of data necessary to establish the safety and / or effectiveness of the new product, such as the effects of changing the drug' s route of administration from topical to oral, are therefore scientifically driven and determined on a case- by- case basis. There can be no assurance that the studies and clinical trials we propose to FDA to establish the safety and effectiveness of GRI- 0621 for the treatment of IPF, or any future candidates we may develop using the 505 (b) (2) NDA pathway, will be deemed sufficient to support all of the differences between our product candidate and the relevant listed drug. For example, we may be required to collect more safety data than we anticipate in order to gain approval of an oral formulation of an active ingredient that has previously been approved by FDA only for topical administration. If the FDA' s interpretation of Section 505 (b) (2) is successfully challenged, or if Congress were to amend the statute to alter the currently available regulatory pathway, the FDA may change its 505 (b) (2) policies and practices, which could delay or even prevent the FDA from approving any NDA we submit under Section 505 (b) (2). In addition, the pharmaceutical industry is highly competitive, and Section 505 (b) (2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs referenced in a Section 505 (b) (2) NDA. Even if we are able to utilize the Section 505 (b) (2) regulatory pathway for one or more of our candidates, there is no guarantee this would ultimately lead to faster product development or earlier approval. Moreover, any delay resulting from our inability to pursue the FDA' s 505 (b) (2) pathway could result in new competitive products reaching the market more quickly than our GRI- 0621 product candidate, which may have a material adverse impact our competitive position and prospects. Even if we are allowed to pursue the FDA' s 505 (b) (2) pathway, we cannot assure you that GRI- 0621 or any of our future product candidates will receive the requisite approvals for commercialization. Risks Related to Regulatory Approval of Our Product Candidates We may seek Fast Track designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not

actually lead to a faster development or regulatory review or approval process. If a product candidate is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, a product sponsor may apply for FDA Fast Track designation. If we seek Fast Track designation for a product candidate, we may not receive it from the FDA. However, even if we receive Fast Track designation, Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular time frame. We may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if the designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA' s priority review procedures. Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review. Maintaining compliance with ongoing regulatory requirements may result in significant additional expense to us, and any failure to maintain such compliance could subject us to penalties and cause our business to suffer. If any of our product candidates are approved, we will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record- keeping, conduct of post- marketing studies and submission of safety, efficacy and other post- market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMPs and GCPs for any clinical trials that we conduct post- approval. Manufacturers and their facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs and applicable ~~tracking and~~ **electronic package-level** tracing requirements. **We** ~~As such, we~~ and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMPs and adherence to commitments made in any marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control. Any **future** regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of **one or more of** our product candidates, which could entail requirements for long-term patient follow- up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves **any of** our product candidates, we will have to comply with requirements including submissions of safety and other post- marketing information and reports and registration. If our original marketing approval for a product candidate was obtained through an accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial in order to confirm the clinical benefit for ~~our~~ **that** ~~products~~ **product** . An unsuccessful post- marketing clinical trial or failure to complete such a trial could result in the withdrawal of marketing approval. We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we hope to obtain marketing approval. The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is not inconsistent with the labeling, and the FDA has recently published a draft guidance with recommendations for how drug manufacturers can share scientifically sound and clinically relevant information on unapproved uses with health care providers so long as such presentations are not promotional. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses and a company that is found to have improperly promoted off- label uses may be subject to significant liability. The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates **(or with drugs that contain the same active ingredients as our product candidates)** , including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post- market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things: • restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls; • new requirements to conduct post-marketing studies or clinical trials; • fines, warning letters or holds on clinical trials; • refusal by the FDA to approve pending applications or supplements to approved applications filed by us; • suspension or revocation of drug product approvals; • voluntary or mandatory product recalls and related publicity requirements; • total or partial suspension of production; • product seizure or detention or refusal to permit the import or export of our product candidates; and • injunctions, consent decrees, or the imposition of civil or criminal penalties **. In addition, adverse side effects caused by any drugs that contain the same active ingredients as or may otherwise be similar in nature to our product candidates could delay or prevent marketing approval of our product candidates or limit the commercial profile of an approved label for our product candidates** . Any government investigation of alleged violations of law would be expected to require us to expend significant time and resources in response and could generate adverse publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to develop and commercialize our products and our value and our operating results would be adversely affected. In addition, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the

adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. Risks Related to Commercialization of our Product Candidates Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third- party payors and others in the medical community necessary for commercial success. Even if GRI- 0621, GRI- 0803 or any other product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients and third- party payors, such as Medicare and Medicaid programs and managed care organizations, and others in the medical community. In addition, the availability of coverage by third- party payors may be affected by existing and future health care reform measures designed to reduce the cost of health care. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including: • efficacy and potential advantages compared to alternative treatments; • the ability to offer our products, if approved, for sale at competitive prices; • convenience and ease of administration compared to alternative treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the recommendations with respect to our product candidates in guidelines published by various scientific organizations applicable to us and our product candidates; • the strength of marketing and distribution support; • the ability to obtain sufficient third- party coverage and adequate reimbursement; and • the prevalence and severity of any side effects, as well as the language and scope of any labeled warnings (including boxed warnings), precautions, or contraindications. Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that out products are safe, therapeutically effective and cost effective as compared with competing treatments. If any product candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product candidate and may not become or remain profitable. If government and other third-party payors do not provide coverage and adequate reimbursement levels for any products we commercialize, market acceptance and commercial success would be reduced. The pricing, coverage, and reimbursement of our approved products, if any, must be sufficient to support our commercial efforts and other development programs, and the availability and adequacy of coverage and reimbursement by third- party payors, including governmental and private insurers, are essential for most patients to be able to afford medical treatments. Sales of our approved products, if any, will depend substantially, both domestically and abroad, on the extent to which the costs of our approved products, if any, will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. If coverage and reimbursement are not available, or are available only in limited amounts, we may have to subsidize or provide products for free or we may not be able to successfully commercialize our products. In addition, there is significant uncertainty related to the insurance coverage and reimbursement for newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the CMS, an agency within HHS, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel product candidates such as ours and what reimbursement codes our product candidates may receive if approved. Outside the United States, international operations are generally subject to extensive governmental price controls and other price- restrictive regulations, and we believe the increasing emphasis on cost- containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of prescription drugs. In many countries, the prices of drugs are subject to varying price control mechanisms as part of national health systems. Price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products, if any. Accordingly, in markets outside the United States, the potential revenue may be insufficient to generate commercially reasonable revenue and profits. Moreover, increasing efforts by governmental and private payors in the United States and abroad to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new drugs and, as a result, they may not cover or provide adequate payment for our products, if any. We expect to experience pricing pressures in connection with drugs due to the increasing trend toward managed healthcare, including the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, and prescription drugs in particular, has and is expected to continue to increase in the future. As a result, profitability of our products, if any, may be more difficult to achieve even if any of them receive regulatory approval. Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize these product candidates outside of the United States, which could limit our ability to realize their full market potential. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties, and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other

countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed. We have no internal sales, marketing, or distribution capabilities. We have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our sales, marketing and distribution capabilities would adversely impact the commercialization of any product candidates that may obtain approval. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over these third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing any approved product candidates that we may have, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses. Healthcare providers, physicians and third- party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third- party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the AKS and the federal False Claims Act, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission (s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. See the section entitled "Item 1. Business — Government Regulation and Product Approval — Other U. S. Healthcare Laws and Regulations." The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource- consuming and can divert a company's attention from other aspects of its business. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, reputational harm, possible exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws. Further, 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 significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Any action for violation of these laws, even if successfully defended, could cause significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example, changes to our manufacturing arrangements; additions or modifications to product labeling; the recall or discontinuation of our products; or additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability. See the section entitled "Item 1. Business — Government Regulation and Product Approval — Pharmaceutical Coverage, Pricing and Reimbursement & Healthcare Reform." Moreover, increasing efforts by governmental and third- party payors in the United States and abroad, including in Canada and Europe, to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U. S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Most recently, in August 2022, President Biden signed into the law the IRA which among other things, contains multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. A manufacturer of drugs or biological products covered by Medicare Parts

B or D must now pay a rebate to the federal government if their drug product' s price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, CMS ~~will~~ **is** ~~negotiate~~ **negotiating** drug prices annually for a select number of single source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities and entered into the first set of agreements with pharmaceutical manufacturers to conduct price negotiations in October 2023 **and ultimately announcing the first round of negotiated prices for the first 10 drugs in August 2024; those negotiated " maximum fair prices " will be effective as of January 1, 2026 (payment year 2026). CMS is currently engaged in its second round of negotiations and published the next 15 drugs selected for negotiation in January 2025** . However, the IRA' s impact on the biopharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e. g., the U. S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. ~~Those~~ -- **The outcome of such ongoing** lawsuits ~~are currently ongoing~~ **, as well as potential legislative changes enacted by Congress or programmatic changes implemented at CMS by the Trump Administration, may impact the IRA drug price negotiation program in the future** . At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third- party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our products or put pressure on our product pricing, which could negatively affect our business, financial condition, results of operations and prospects. In addition, the U. S. Supreme Court held unanimously in December 2020 that federal law does not preempt the states' ability to regulate PBMs and other members of the health care and pharmaceutical supply chain, an important decision that has led to further and more aggressive efforts by states in this area. The FTC in mid- 2022 also launched sweeping investigations into the practices of the PBM industry **, and published interim reports with its findings in mid- 2024 and January 2025,** that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements **, including in the current 2025- 2026 congressional session** . Both the U. S. Congress and state legislatures are increasingly scrutinizing the industry and proposing novel regulatory approaches to address various perceived public policy concerns. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including biopharmaceutical product developers like us. Further, in September 2023, the FTC issued a policy statement articulating its view that certain " improper " patent listings by drug developers in FDA' s Orange Book represent an unfair trade practice and indicated that industry should be prepared for potential enforcement actions based on its analysis. The FTC followed that action in November 2023 by publicly calling out over 100 " improper " patent listings made by ten large pharmaceutical companies and initiating an FDA administrative process with respect to those patents. **The controversy regarding the appropriateness of listing such patents has led to numerous lawsuits alleging anticompetitive conduct by biopharmaceutical companies.** It remains to be seen whether the FTC ~~,~~ **under** ~~other~~ -- **the Trump Administration will** ~~governmental agencies, pharmaceutical manufacturers, or other stakeholders~~ continue to prioritize the policy issue of " improper " patent listings ~~and~~ **or** whether ~~significant litigation will develop in~~ **Congress may take any legislative actions related to** this ~~area~~ **issue** . Accordingly, regulatory and government interest in biopharmaceutical industry business practices continues to expand and pose a risk of uncertainty. These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Additionally, we expect to experience pricing pressures in connection with the sale of any future approved product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including from December 22, 2018 through January 25, 2019, the U. S. government has shut down several times, and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC, and other government employees and stop critical activities. If a prolonged government shutdown or slowdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. There have been U. S. government shutdowns historically, and recent government shutdowns have been threatened; it is often unclear how long a shutdown will last and what impacts it may have on the federal agencies that have jurisdiction over our various operations **. In addition, three decisions from the U. S. Supreme**

Court issued in July 2024 may lead to an increase in litigation against regulatory agencies that could create uncertainty and thus negatively impact our business. The first decision overturned established precedent that required courts to defer to regulatory agencies' interpretations of ambiguous statutory language. The second decision overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. The third decision extended the statute of limitations within which entities may challenge agency actions. These cases may result in increased litigation by industry against regulatory agencies, including but not limited to the FDA and SEC, and may impact how such agencies choose to pursue enforcement and compliance actions. However, the specific, lasting effects of these decisions, which may vary within different judicial districts and circuits, is unknown. We also cannot predict the extent to which FDA and SEC regulations, policies, and decisions may become subject to increasing legal challenges, delays, and changes . We are subject to certain U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations. Among other matters, United States. and foreign anti-corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations (collectively, Trade Laws) prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities and other organizations. We also expect our non- U. S. activities to increase in time. We plan to engage third parties for clinical trials and / or to obtain necessary permits, licenses, patent registrations and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. Our research and development activities and our third- party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations; environmental damage resulting in costly clean- up; and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by us and our third- party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of specified materials and / or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry hazardous waste insurance coverage. Our business depends in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, synthetic intermediates, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third- party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected. The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. The patenting process is subject to numerous risks and there can be no assurance that we will be successful in obtaining patents for which we have applied. In addition, we may not pursue, obtain, or maintain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees. The strength of patents in the biotechnology and biopharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in- license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our product candidates, or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. We cannot be certain that we were the first to file any patent application related to our technology, including our product candidates, and, if we were not, we may be precluded from obtaining patent protection for our technology, including our product candidates. We cannot be

certain that we were the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. Furthermore, for U. S. applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third- party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, for U. S. applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor' s disclosure. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our product candidates, or would be found by a court to be infringed by a competitor' s technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and consider that we are free to operate in relation to our product candidates, but our competitors may obtain issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights or will design around the claims of patents that may issue that cover our products. The degree of future protection for 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. In connection with our efforts to expand our pipeline of product candidates, we may enter into certain licenses or other collaboration agreements pertaining to the in- license of rights to additional product candidates. Such agreements may impose various diligence, milestone payment, royalty, insurance, or other obligations on us. If we fail to comply with these obligations, our licensor or collaboration partners may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licensed intellectual property. Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights under our collaborative development relationships; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the inventorship and ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and • the priority of invention of patented technology. In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. In addition, we may have limited control over the maintenance and prosecution of these in- licensed patents and patent applications, or any other intellectual property that may be related to our in- licensed intellectual property. For example, we cannot be certain that such activities by any future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third- party infringer of the intellectual property rights or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding, or defense activities may be less vigorous than had we conducted them ourselves. Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and / or proprietary technologies infringe their intellectual property rights. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies, or methods. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our Common Stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of complex patent litigation more

effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition, and prospects. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. Third parties may assert that we are employing their proprietary technology without authorization. There may be third- party patents of which we are currently unaware with claims to compositions of matter, materials, formulations, methods of manufacture or methods for treatment that encompass the composition, use or manufacture of our product candidates. There may be currently pending patent applications of which we are currently unaware which may later result in issued patents that our product candidates or their use or manufacture may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patent were held by a court of competent jurisdiction to cover our product candidates, intermediates used in the manufacture of our product candidates or our materials generally, aspects of our formulations or methods of manufacture or use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third- party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly. Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets. As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our Common Stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace. Others may claim an ownership interest in our intellectual property, which could expose us to litigation and have a significant adverse effect on our prospects. A third - party may claim an ownership interest in one or more of our or our licensors' patents or other proprietary or intellectual property rights. A third - party could bring legal actions against us and seek monetary damages and / or enjoin clinical testing, manufacturing and marketing of the affected product or products. While we are presently unaware of any claims or assertions by third parties with respect to our patents or other intellectual property, we cannot guarantee that a third - party will not assert a claim or an interest in any of such patents or intellectual property. If we become involved in any litigation, it could consume a substantial portion of our resources and cause a significant diversion of effort by our technical and management personnel. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license to continue to manufacture or market the affected product, in which case we may be required to pay substantial royalties or grant cross- licenses to our patents. We cannot predict whether any such license will be available on commercially acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product candidate or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts

may reasonably disagree. We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in- license or use these proprietary rights. Our product candidates may also require specific formulations to work effectively and efficiently, and these rights may be held by others. We may develop products containing our compounds and pre- existing biotechnology and biopharmaceutical compounds. We may be unable to acquire or in- license any compositions, methods of use, processes, or other third- party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third- party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. The licensing and acquisition of third- party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third- party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, or challenging the patent rights of others, which could be expensive, time- consuming and unsuccessful. Competitors or other third parties such as chemical and reagent suppliers may infringe our patents or the patents of our current or future licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question or for other reasons. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We may choose to challenge the patentability of claims in a third- party' s U. S. patent by requesting that the USPTO review the patent claims in an ex- parte re- examination, inter partes review or post- grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third- party' s patent in patent opposition proceedings in the European Patent Office (EPO) or other foreign patent offices. The costs of these opposition proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent offices, we may be exposed to litigation by a third- party alleging that the patent may be infringed by our product candidates or proprietary technologies. In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in- licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent or first to file a patent application covering the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in- licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U. S. patent application on inventions similar to those owned by or in- licensed to us, we or, in the case of in- licensed technology, the licensor may have to participate in an interference or derivation proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference or derivation proceeding involving a U. S. patent application on inventions owned by or in- licensed to us, we may incur substantial costs, divert management' s time and expend other resources, even if we are successful. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non- exclusive license is offered and our competitors gain access to the same technology. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our Common Stock. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other

governmental fees on our owned and in- licensed issued patents and patent applications are or will be due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. In certain circumstances, even inadvertent noncompliance events may permanently and irrevocably jeopardize patent rights. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business. Any patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO (or foreign patent offices). If we or one of our licensors initiate legal proceedings against a third- party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace, and there are numerous grounds upon which a third- party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates. Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. We own pending patent applications covering our proprietary technologies or our product candidates that if issued as patents are expected to expire from 2032 through 2035, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO, EPO or other relevant foreign patent offices will grant any of these patent applications. Changes in patent law in the United States and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. Changes in either the patent laws or interpretation of the patent laws in the United States or in foreign jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 16, 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. On March 16, 2013, under the Leahy- Smith America Invents Act (the America Invents Act), the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third - party was the first to invent the claimed invention. A third - party that files a patent application in the USPTO on or after March 16, 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third - party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor' s patents or patent applications. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third - party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including post- grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U. S. federal courts necessary to invalidate a patent claim, a third - party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third - party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third - party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in- licensed patent applications and the enforcement or defense of our owned or in- licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. In addition, the patent positions of companies in the development and commercialization of biotechnology and biopharmaceuticals are particularly uncertain. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U. S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our

ability to protect and enforce our intellectual property in the future. We have limited foreign intellectual property rights and may not be able to protect and enforce our intellectual property rights throughout the world. We have limited intellectual property rights outside the United States. Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of, and may require a compulsory license to, patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology and biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. If we do not obtain patent term extension and data exclusivity or similar non- U. S. legislation extending the term of protection covering any product candidates we may develop, our business may be materially harmed. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U. S. patents may be eligible for limited patent term extension under the Hatch- Waxman Act. The Hatch- Waxman Act permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents, or otherwise failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, within the EU, regulatory protections afforded to medicinal products such as data exclusivity, marketing protection, market exclusivity for orphan indications and pediatric extensions are currently under review and could be curtailed in future years. If we are unable to obtain patent term extension or the term of any such extension is less than we request, or if data exclusivity or other regulatory protections are reduced, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed. We have relied upon and plan to continue to rely upon third- party CROs to conduct, monitor and manage our clinical programs. We rely on these parties for execution of clinical trials and we manage and control only some aspects of their activities. We remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable laws, regulations and guidelines, including those required by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. If we, or any of our CROs or vendors, fail to comply with applicable laws, regulations or guidelines, **or as otherwise required,** the results generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot be assured that our CROs or other vendors will meet these requirements, or that upon inspection by any regulatory authority, such regulatory authority will determine that efforts, including any of our clinical trials, comply with applicable requirements. Our failure to comply with these laws, regulations or guidelines may require us to repeat clinical trials, which would be costly and delay the regulatory approval process. If any of our relationships with these third- party CROs terminates, or they otherwise are subject to quarantines, shelter-in- place orders, shutdowns or other restrictions and must scale back their operations unexpectedly we may not be able to enter into arrangements with alternative CROs in a timely manner or do so on commercially reasonable terms. In addition, our CROs may not prioritize our clinical trials relative to those of other customers, and any turnover in personnel or delays in the allocation of CRO employees by the CRO may negatively affect our clinical trials. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, our clinical trials may be delayed or terminated, and we may not be able to meet our current plans with respect to our product candidates. CROs also may involve higher costs than anticipated, which could negatively affect our financial condition and operations. In addition, we rely on third- party manufacturers to produce our

clinical- stage product candidates, and their responsibilities often include purchasing from third- party suppliers the materials necessary to produce our product candidates for our clinical trials and regulatory approval. ~~We expect there~~ **There are** ~~to be~~ a limited number of suppliers for some of the raw materials that we expect to use to manufacture our product candidates, and we may not be able to identify alternative suppliers to prevent a possible disruption of the manufacture of our product candidates for our clinical trials, and, if approved, ultimately for commercial sale. Although we generally do not expect to begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the trial, any significant delay or discontinuity in the supply of a product candidate, or the raw materials or other material components in the manufacture of the product candidate, could delay completion of our clinical trials and potential timing for regulatory approval of our product candidates, which would harm our business and results of operations. We do not yet have sufficient information to reliably estimate the cost of the commercial manufacturing of our product candidates and our current costs to manufacture our product candidates may not be commercially feasible. As a result, we may never be able to develop a commercially viable product. In addition, our reliance on third- party manufacturers exposes us to the following additional risks: • we may be unable to identify manufacturers to manufacture our product candidates on acceptable terms or at all, because the number of qualified potential manufacturers is limited. Following NDA approval, a change in the manufacturing site could require additional approval from the FDA. This approval would require new testing and compliance inspections; • our third- party manufacturers might be unable to timely formulate and manufacture our product or produce the quantity and quality required to meet our clinical and commercial needs, if any; • our third- party manufacturers might be forced to scale back or terminate operations as a result of labor shortages, inflation, natural disasters or geopolitical conflicts, which could harm our ability to conduct ongoing and future clinical trials of our product candidates; • our future third- party manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our product candidates; • drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMPs and other government regulations and corresponding foreign standards, and we do not have control over third- party manufacturers' compliance with these regulations and standards; • if any third- party manufacturer makes improvements in the manufacturing process for our products, we may not own or be able to license, or we may have to share, the intellectual property rights to any improvements made by our third- party manufacturers in the manufacturing process for our product candidates; and • our third- party manufacturers could breach or terminate their agreements with us. Each of these risks could delay our clinical trials, the approval, if any, of our product candidates, or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenue. In addition, we rely on third parties to perform release testing on our product candidates prior to delivery to subjects in our clinical trials. If these tests are not appropriately conducted and test data are not reliable, subjects in our clinical trials, or patients treated with our product candidates, if any are approved in the future, could be put at risk of serious harm, which could result in product liability suits. Our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants or vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities to us that violates: FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; manufacturing standards; federal and state healthcare fraud and abuse laws and regulations; or laws that require the true, complete and accurate reporting of financial information or data. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished potential profits and future earnings, and curtailment of our operations, any of which could adversely affect our business, financial condition, results of operations or prospects. We rely on third- party contract manufacturers to manufacture our product candidates for preclinical studies and clinical trials. We do not own manufacturing facilities for producing any clinical trial product supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited or interrupted, or that they will be of satisfactory quality or continue to be available at acceptable prices. The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. 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. In the event that any of our manufacturers fails to comply with these requirements or to perform its obligations to us 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 manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third - party, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer

and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to a back- up or alternative supplier, or we may not be able to transfer such skills or technology at all. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third **-** party manufacture our product candidates. We **currently** rely on a sole supplier ~~or, in some cases, a limited number of suppliers,~~ for the manufacture of GRI- 0621 ~~, GRI- 0803 and our other product candidates~~ . If ~~these~~ **this** ~~suppliers~~ **supplier** ~~are~~ **is** unable to supply to us in the quantities we require, or at all, or otherwise ~~default~~ **defaults** on their supply obligations to us, we may not be able to obtain alternative supplies from other suppliers on acceptable terms, in a timely manner, or at all. Moreover, in the event **this** ~~any of these suppliers~~ **supplier** ~~breach~~ **breaches** ~~their~~ **its** contracts with us, our legal remedies associated with such a breach may be insufficient to compensate us for any damages we may suffer. In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturer or manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. We expect to continue to rely on third- party manufacturers if we receive regulatory approval for GRI- 0621, GRI- 0803 or any other 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. 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. A part of our strategy is to consider partnerships in indications and geographies where we believe partners can add significant commercial and / or development capabilities. Further, we do not yet have any capability for commercialization. Accordingly, we have and may in the future enter into collaborations with other companies to provide us with important technologies and funding for our programs and technology. Any future collaborations we enter into may pose a number of risks, including that collaborators have significant discretion in determining the efforts and resources that they will apply and may not perform their obligations as expected, collaborators may not provide us with timely and accurate information regarding development progress and activity under any future license agreement, which could adversely impact our ability to report progress to our investors and otherwise plan development of our product candidates, we may have disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time- consuming and expensive and collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. We face significant competition in seeking appropriate collaborators for our product candidates, and the negotiation process is time- consuming and complex. In order for us to successfully establish a collaboration for one or more of our product candidates, potential collaborators must view these product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Collaborations are complex and time- consuming to negotiate and document. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into future collaborations or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue from sales of drugs or continue to develop our technology, and our business may be materially and adversely affected. Even if we are successful in our efforts to establish new strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. Our ability to compete in the highly competitive biotechnology and biopharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our management, scientific and medical personnel, including W. Marc Hertz, our President and Chief Executive Officer, Vipin Kumar Chaturvedi, our Chief Scientific Officer and Albert Agro, our Chief Medical Officer **. We have modified our employment arrangements with Dr. Agro. On June 16, 2024, our board of directors approved an amendment to Dr. Agro' s employment agreement, which reduced Dr. Agro' s service for us to at least 70 hours per month. Dr. Agro may devote the balance of his time to other consulting or employment activities** . The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business. We conduct our operations at our facility in La Jolla, California. This region is headquarters to many other biotechnology companies, biopharmaceutical companies, and research institutions. Competition for skilled personnel in our market is intense and may limit

our ability to hire and retain highly qualified personnel on acceptable terms or at all. To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity awards that vest over time. The value to employees of equity awards that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Our key employees are at- will employees, which means that any of our employees could leave our employment at any time, with or without notice. There is no guarantee that any " key person " insurance policy we have or may enter into would adequately compensate us for the loss of any key employee. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid- level and senior scientific and medical personnel. If we fail to attract and retain management and other key personnel, we may be unable to successfully develop or commercialize our product candidates or otherwise implement our business plan. The ~~biotech~~ **biotechnology** industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive biopharmaceuticals industry depends upon our ability to attract, retain, and motivate highly skilled and experienced personnel with scientific, medical, regulatory, manufacturing, and management skills and experience. We may not be able to attract or retain qualified personnel in the future due, in part, to the intense competition for a limited number of qualified personnel among biopharmaceutical companies. Many of the other biopharmaceutical companies against which we will compete have greater financial and other resources, different risk profiles, and a longer history in the industry. Our competitors may provide higher compensation, more diverse opportunities, and / or better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize our product candidates and to grow our business and operations as currently contemplated. ~~Our~~ **We may be unable to adequately protect our internal information systems, or those used by our CROs, clinical sites, or other contractors or consultants upon which we rely, from cyberattacks, compromises, cybersecurity incidents, or other disruptions, compromises, cybersecurity incidents, or other disruptions, which could result in the compromise of sensitive or proprietary information, lead to operational or service interruption, harm our reputation, and subject us to litigation, fines and other significant financial and legal exposure, and other material and adverse consequences. In the ordinary course of our business, we, and the third parties upon which we rely, process sensitive or proprietary information and as a result, we and the third parties upon which we rely face a variety of evolving threats which could cause material cybersecurity incidents. Despite our implementation of security measures, our** internal computer systems and those of ~~any future~~ **our CROs, clinical sites, and other** collaborators **,** ~~and other~~ contractors **,** or consultants **upon which we rely** are vulnerable to ~~damage from~~ **cyberattacks,** computer viruses **, malware, bugs, worms, or other malicious code, software or hardware failures, loss of data or other information technology assets** , phishing or other unauthorized access, natural disasters, terrorism, war **,** and telecommunication and electrical failures **, and other similar threats. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer " hackers, " threat actors, " hacktivists, " organized criminal threat actors, personnel, such as through theft or misuse, sophisticated nation states, and nation- state- supported actors. In particular, ransomware attacks, including those from organized criminal threat actors, nation- states and nation- state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, loss of data, including significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the negative impact of a ransomware attack, it may be preferable to make payments to the threat actor (s), but we may be unwilling or unable to do so, including, for example, if applicable laws or regulations prohibit such payments. Some threat actors also now engage and are expected to continue to engage in cyber- attacks, including without limitation nation- state actors, for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, the third parties upon which we rely, and our customers may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks that could materially disrupt our systems and operations. In addition to experiencing a cybersecurity incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or research and development activities. Additionally, remote work has become more common and has increased risks to our information technology systems and data, as our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations. While we take steps to detect and remediate vulnerabilities, we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit such vulnerabilities change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a cybersecurity incident has occurred, if at all. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. We rely on third- party service providers and critical business information technology systems that we or our third- party service providers operate to process, transmit and store confidential, sensitive, and proprietary information in our day- to- day operations. We also rely on third- party service providers to assist with our clinical trials, provide other products or services, or otherwise to operate our research and development activities. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third- party service providers experience a cybersecurity incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third- party service providers fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition and in general, supply- chain attacks have increased in frequency and**

severity, and we cannot guarantee that third parties and infrastructure in our supply chain or our third- party partners' supply chains have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems, including our services, or the third- party information technology systems that support us and our services. Any of the previously identified or similar threats could cause a cybersecurity incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive data or our information technology systems, or those of the third parties upon whom we rely. A cybersecurity incident or other interruption could materially and adversely disrupt our ability, and that of third parties upon whom we rely, to conduct clinical trials and our research and development activities. The costs related to significant cybersecurity breaches or disruptions could be material and cause us to incur significant expenses. If the information technology systems of our CROs, clinical sites, and other contractors and consultants become subject to disruptions or cybersecurity incidents, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring . If such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our ~~business~~ operations, financial loss, a loss of our trade secrets or other proprietary information and damage to our reputation and otherwise negatively impact us. For example, the loss of clinical trial data from **ongoing or** future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or ~~security~~ **cybersecurity** ~~breach~~ **incident** were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential **, sensitive,** or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed. ~~We rely on information technology systems that we or~~ **Applicable data privacy and security obligations may require us to notify relevant stakeholders, regulatory authorities, and other individuals of cybersecurity incidents, and take other remedial measures. Such disclosures and measures are costly, and the disclosure** ~~our~~ **or the failure** ~~third- party providers operate~~ to **comply** ~~process, transmit and store electronic information in our day- to- day operations. In connection~~ with ~~our product discovery efforts, we may collect and use a variety of personal data,~~ such **requirements** ~~as names, mailing addresses, email addresses, phone numbers and clinical trial information. A successful cyberattack~~ could **lead to adverse consequences. Any such event could also** result in ~~the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial of service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business,~~ legal **claims** ~~, financial or reputational harm to us, or would have a material adverse effect on our~~ **or proceedings** ~~results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to , use of, or disclosure of personal data, including study participant personal data could result in significant~~ liability under ~~state (e. g., state breach notification~~ laws **that protect** ~~), federal (e. g., Section 5 of~~ the ~~FTC Act),~~ **privacy of personal information** and **significant regulatory penalties** ~~international (e. g., the GDPR) law~~ and **damage** ~~may cause a material adverse impact~~ to our reputation ~~, affect~~ **and a loss of confidence in us and** our ability to conduct **clinical trials** ~~our studies and potentially disrupt our business. We rely on our third- party providers to implement effective security measures and identify and correct for any such failures , deficiencies or breaches. If we or our third- party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third- party providers could have difficulty preventing, detecting and controlling such cyberattacks, and any such attacks could result in the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues, civil liability or other adverse consequences, any of~~ which could **delay** ~~have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business. By way of example, the CCPA, which went into effect on January 1, 2020, creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches increasing the potential for data breach litigation. The CPRA became effective on January 1, 2023 to strengthen elements of the CCPA. While there~~ -- **the** ~~are exceptions for information that is subject to HIPAA and~~ clinical **development** ~~trial regulations, the CCPA, as applicable, would still impact our business, and may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and actually implemented in other states. By way~~ of ~~example regarding foreign laws and regulations with respect to data privacy and security, the GDPR went into effect in the EU in May 2018 introducing strict requirements for processing the personal data of EU data subjects. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or~~ **our product candidates** ~~4 % of the annual global revenues of the noncompliant company, whichever is greater~~ . Our current

operations are concentrated in one location, and we or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster, including earthquakes, outbreak of disease or other natural disasters. Our current operations are located in our facilities in La Jolla, California. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical ~~epidemics~~ **epidemic**, power shortage, telecommunication failure or other natural or manmade ~~accidents~~ **accident** or ~~incidents~~ **incident** that ~~result~~ **results** in us being unable to fully utilize our facilities, or the manufacturing facilities of our third- party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Some of these natural events may be exacerbated by climate change. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption **or disruption** of our business operations **, all of which** ~~. Earthquakes or other natural disasters~~ could ~~further disrupt our operations and~~ have a material and adverse effect on our business, financial condition, results of operations and prospects ~~. In addition, global climate change could result in certain types of natural disasters occurring more frequently or with more intense effects~~. If a natural disaster, power outage or other event occurred that prevented **or interrupted** us from using all or a significant portion of our headquarters, ~~that~~ damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third- party contract manufacturers, or ~~that~~ otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans **and procedures** we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of ~~the limited nature~~ **any failure or inadequacy** of our disaster recovery and business continuity plans **and procedures**, which, could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at **reasonable** levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of **our** insurance **coverage** will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third- party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed **or delayed**. Our business could be adversely affected by the effects of health pandemics or epidemics in regions where it or third parties on which it relies have significant manufacturing facilities, concentrations of clinical trial sites, or other business operations. Our business could be adversely affected by the effects of health pandemics or epidemics in regions where it has concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third- party manufacturers and CROs upon whom it relies. Such pandemics or epidemics may negatively impact productivity, disrupt business and delay clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of any restrictions and other limitations placed on our ability to conduct business in the ordinary course as a result of any such pandemic or epidemic. These and similar disruptions in operations could negatively impact our business, operating results and financial condition. Quarantines, stay at home and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, may impact personnel at third- party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which could disrupt our supply chain. While many of these materials may be obtained by more than one supplier, restrictions resulting from any pandemic may disrupt our supply chain or limit our ability to obtain sufficient materials for our product candidates. Our insurance may not provide adequate levels of coverage against claims which may adversely affect our financial condition. We maintain insurance that we believe is adequate for businesses of our size and type. However, there are types of losses that we believe are not economically reasonable to insure or that cannot be insured against. It is possible that we may be subject to securities litigation in the future, including potential class action or stockholder derivative actions. Our indemnification agreements with our directors and certain officers, as well as Delaware General Corporation Law (DGCL), may require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. Without ~~D & O~~ **Director and Officer** insurance, the amounts we would pay to defend any such litigation or indemnify our officers and directors should they be subject to legal action based on their service to us could have a material adverse effect on our financial condition, results of operations and liquidity. Risks Related to Our Common Stock, Financing and Capital Requirements The market price of shares of our Common Stock has been and is likely to continue to be subject to significant fluctuations. Market prices for securities of biotechnology and other life sciences companies historically have been particularly volatile subject even to large daily price swings. Some of the factors that may cause the market price of shares of our Common Stock to fluctuate include, but are not limited to: • our ability to obtain timely regulatory approvals for future product candidates, and delays or failures to obtain such approvals; • our ability to comply with the listing requirements of The Nasdaq Capital Market and any delisting or potential delisting of shares of our Common Stock; • failure of product candidates, if approved, to achieve commercial success; • issues in manufacturing future product candidates; • the results of current and any future clinical trials; • the entry into, or termination of, or breach by partners of key agreements, including key commercial partner agreements; • the initiation of, material developments in, or conclusion of any litigation to enforce or defend any intellectual property rights or defend against the intellectual property rights of others; • announcements of any dilutive equity financings and significant issuances of equity securities; • announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships or capital commitments; • failure to elicit meaningful stock analyst coverage and downgrades of our stock by analysts; • our ability to comply with our obligations pursuant to our registration rights agreements; and • the loss of key employees. Moreover, the stock markets in general have experienced substantial volatility in the ~~biotech~~ **biotechnology** industry that has often been unrelated to the operating performance of individual companies or a certain industry segment. These broad market fluctuations may also adversely affect the trading price of our Common Stock. In the past, following periods of volatility in the market price of a company' s securities,

stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation. In addition, such securities litigation often has ensued after a reverse merger or other merger and acquisition activity of the type engaged by us. Such litigation, if brought, could impact negatively our business. We expect that significant additional capital will be needed in the future to continue our planned operations, including research and development, increased marketing, hiring new personnel, commercializing our products, and continuing activities as an operating public company. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell shares of our Common Stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell Common Stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. As of December 31, ~~2023~~ **2024** , there were a total of (i) **420** ~~530, 375~~ shares of Common Stock directly or indirectly underlying the ~~Equity~~ **Series B- 1 common warrants (the Series B- 1 Common** Warrants **) and Series B- 2 common warrants** (~~including (i~~ **the Series B- 2 Common Warrants, and together with the Series B- 1 Common Warrants, the Series B Common Warrants**) ~~116~~ , ~~353 shares of Common Stock underlying Series A- 1 Warrants to purchase shares of Common Stock, which Series A- 1 Warrants are issuable upon exercise of Series T Warrants, assuming that the Series T Warrants have been exercised in full by paying the aggregate exercise price in cash and~~ (ii) ~~116~~ **257** , ~~353~~ **154** shares of Common Stock **directly or indirectly** underlying **the** Series ~~A~~ **C- 1 common warrants (the Series C- 1 Common Warrants) and Series C** - 2 **common warrants (the Series C- 2 Common** Warrants ~~to purchase shares of~~ **, and together with the Series C- 1** Common ~~Stock~~ **Warrants** , ~~which~~ **the** Series **C Common** ~~A- 2~~ Warrants ~~are issuable upon exercise of Series T Warrants, assuming that the Series T Warrants have been exercised in full by paying the aggregate exercise price in cash~~), (iii) ~~4~~ **89** , ~~576~~ **678 shares of Common Stock directly or indirectly underlying the Series D- 1 common warrants (the Series D- 1 Common Warrants) and Series D- 2 common warrants (the Series D- 2 Common Warrants, and together with the Series D- 1 Common Warrants, the Series D Common Warrants), (iv) 12, 171** shares of Common Stock underlying other outstanding warrants to purchase Common Stock, (~~iv~~ **v**) **62** ~~4, 318~~ shares of Common Stock issuable upon the exercise of vested outstanding options under the Amended and Restated GRI Bio ~~, Inc. 2018 Equity Incentive Plan, formerly the Vallon Pharmaceuticals~~ , Inc. 2018 Equity Incentive Plan (the A & R 2018 Plan), ~~and~~ (~~v~~ **vi**) an additional **80** ~~28, 324~~ shares of Common Stock issuable upon the exercise of options that remain subject to vesting as of that date and ~~no~~ **(vii) 114** options available for future issuance under the ~~GRI Bio, Inc. 2015 Equity Incentive Plan (the GRI Operations Plan) or the~~ A & R 2018 Plan ~~. In connection with the issuance of the securities pursuant to the Purchase Agreement the exercise price of the Series A- 1 Warrants was reduced to par, or $ 0. 0001, per share pursuant to the terms of the Series A- 1 Warrants. As of December 31, 2023, an aggregate of 60, 227 shares of our Common Stock have been issued upon the exercise of Exchange Warrants and an aggregate of 163, 185 shares of our Common Stock have been issued upon the exercise of Series A- 2 Warrants, in each case, on a cashless basis for which the Company received no proceeds~~ . We will not receive any proceeds from the exercise of warrants to the extent exercised on a cashless basis. The holders of these securities or their affiliates have and may sell large amounts of our Common Stock in the open market or in privately negotiated transactions, which, in the past and again may result in a lower trading price of our Common Stock and substantial dilution to our stockholders. Additionally, the registration and availability of such a significant number of shares of Common Stock for trading in the public market has and may increase the volatility in our stock price or put significant downward pressure on the price of our **Common** ~~stock~~ **Stock** . We do not anticipate paying any dividends in the foreseeable future. Our current expectation is that we will retain our future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of the shares of our Common Stock will be our stockholders' sole source of gain, if any, for the foreseeable future. We will continue to incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives. In addition, if we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired. As a public company, we incur significant legal, accounting and other expenses under the Exchange ~~Ac~~ **Act** ~~)~~ , the Sarbanes- Oxley Act of ~~2022~~ - **2002** , as amended (SOX) and other applicable securities rules and regulations. In addition, we are subject to the rules of ~~The~~ Nasdaq ~~Stock Market LLC (Nasdaq)~~ and The Nasdaq Capital Market. These rules impose various requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and appropriate corporate governance practices. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time- consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. In addition, the listing requirements of The Nasdaq Capital Market require that we satisfy certain corporate governance requirements relating to director independence, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel need to devote a substantial amount of time to ensure that we comply with all of these requirements. As a result, it may be difficult for us to attract and retain qualified persons to serve on our Board, our Board committees or as executive officers. SOX requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. As a result, we are required to periodically perform an evaluation of our internal controls over financial reporting to allow management to report on the effectiveness of those controls, as required by Section 404 of SOX (Section 404). Additionally, our independent auditors may be required to perform a similar evaluation and report on the effectiveness of our internal controls over financial reporting. These efforts to comply with Section 404 and related regulations have required, and continue to require, the commitment of significant financial and managerial resources. **Based on**

management' s processes and assessment, as described under Item 9A. " Controls and Procedures, " management has concluded that, as of December 31, 2024, our internal control over financial reporting was not effective as a result of material weakness related to inaccurate computation of the non- cash deemed dividend associated with the pre- pricing of the Series B Common Warrants in the Warrant Pricing Transaction (as defined below) in accordance with applicable GAAP guidance. While we anticipate **remediating this material weakness, and** maintaining the integrity of our internal controls over financial reporting and all other aspects of Section 404, we cannot be certain that ~~a~~ **additional** material ~~weakness~~ **weaknesses** will not be identified when we test the effectiveness of our control systems in the future **or that our remediation efforts will be or remain successful** . If ~~a~~ **additional** material ~~weakness~~ **weaknesses** ~~is~~ **are** identified, we could be subject to sanctions or investigations by the SEC, or other regulatory authorities, which would require additional financial and management resources, costly litigation or a loss of public confidence in our internal controls, which could have an adverse effect on the market price of our stock **. Notwithstanding this material weakness, we believe that our financial statements contained in this Annual Report on Form 10- K fairly present our financial position, results of operations and cash flows for the periods covered by this report in all material respects** . We currently take advantage of reduced disclosure and governance requirements applicable to smaller reporting companies, which could result in our Common Stock being less attractive to investors. We have a public float of less than $ 250. 0 million and therefore qualify as a smaller reporting company under the rules of the SEC. As a smaller reporting company, we are able to take advantage of reduced disclosure requirements, such as simplified executive compensation disclosures and reduced financial statement disclosure requirements in our SEC filings. Decreased disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our Common Stock less attractive if we rely on these exemptions. If some investors find our Common Stock less attractive as a result, there may be a less active trading market for our Common Stock and our stock price may be more volatile. We may take advantage of the reporting exemptions applicable to a smaller reporting company until we are no longer a smaller reporting company, which status would end once we have a public float greater than $ 250. 0 million. In that event, we could still be a smaller reporting company if our annual revenues were below $ 100. 0 million and we have a public float of less than $ 700. 0 million. We also take advantage of reduced disclosure and governance requirements applicable to emerging growth companies, which could result in our Common Stock being less attractive to investors. We are an " emerging growth company, " as defined in the JOBS Act. Emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. As an emerging growth company, we are not being required to comply with the auditor attestation requirements of Section 404, we have reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and we are exempt from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. Additionally, as an emerging growth company, we have elected to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. As such, our financial statements may not be comparable to companies that comply with public company effective dates. We cannot predict if investors will find our stock less attractive because we may rely on these provisions. If some investors find our stock less attractive as a result, there may be a less active trading market for our shares and our stock price may be more volatile. Further, Section 102 (b) (1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies (that is, those that have not had a **registration statement filed under the** Securities Act ~~registration statement~~ **of 1933, as amended (the Securities Act))** declared effective or do not have a class of securities registered under the Exchange Act) are required to comply with the new or revised financial accounting standards. The JOBS Act provides that a company can elect to opt out of the extended transition period and comply with the requirements that apply to non- emerging growth companies but any such an election to opt out is irrevocable. We have elected not to opt out of such extended transition period which means that when a standard is issued or revised and it has different application dates for public or private companies, we, as an emerging growth company, will not adopt the new or revised standard until the time private companies are required to adopt the new or revised standard. This may make comparison of our financial statements with another public company which is neither an emerging growth company nor an emerging growth company which has opted out of using the extended transition period difficult or impossible because of the potential differences in accountant standards used. We will remain an emerging growth company until the earliest of (i) the end of the fiscal year in which the market value of our common stock that is held by non- affiliates exceeds $ 700 million as of the end of the second fiscal quarter, (ii) the end of the fiscal year in which we have total annual gross revenues of $ 1. 235 billion or more during such fiscal year, (iii) the date on which we issue more than $ 1 billion in non- convertible debt in a three- year period, or (iv) the end of the fiscal year following the fifth anniversary of the date of the first sale of our common stock pursuant to an effective registration statement filed under the Securities Act **(December 31, 2026)** ~~. The listing of shares of our Common Stock does not currently comply with the rules of The Nasdaq Capital Market or any other Nasdaq Market tier~~ . A delisting of our Common Stock from Nasdaq could adversely affect our ability to raise additional capital through the public or private sale of equity securities and our investors' ability to dispose of, or obtain accurate quotations as to the market value of, our Common Stock. The rules of The Nasdaq Capital Market ~~also~~ require that we maintain a closing price for shares of our Common Stock of at least $ 1. 00 per share (the Minimum Bid Price Rule) **and that we meet other requirements for continued listing which include, among other things, requirements that we maintain a market value of listed securities of at least $ 35 million or, alternatively, stockholders' equity of at least $ 2. 5 million, or, alternatively, annual net income from continuing operations of at least $ 500 thousand as described in applicable listing requirements. As of the date of this Annual Report, the market value of our listed securities was less than $ 35 million, and we had not earned net income in excess of $ 500 thousand. We will need to raise a substantial amount of capital in the near term to maintain compliance with The Nasdaq Capital Market' s $ 2. 5**

million equity requirement and these efforts may not be successful . On ~~January 5~~ **September 10** , 2024, we received a letter (the Letter) from the Staff of Nasdaq indicating that we no longer met the Minimum Bid Price Rule set forth in Nasdaq Listing Rule 5550 (a) (2) because the closing bid price for our Common Stock was less than $ 1. 00 for the ~~previous~~ 30 consecutive business days **prior thereto** . ~~The~~ **On February 19, 2025, we filed an amendment to our Charter to implement a reverse split of our Common Stock at a ratio of one- for- seventeen (the February 2025 Reverse Stock Split) to attempt to regain compliance with the Minimum Bid Price Rule. Subsequently, on March 10, 2025, we received a letter from the Staff indicating that we were once again in compliance with the Minimum Bid Price Rule. However, we may fail to maintain long- term compliance with the Minimum Bid Price Rule. We previously effected two reverse stock splits in 2024 prior to receiving the** Letter ~~was~~ **from Nasdaq** in **September 2024** ~~addition to the Notice (as defined below)~~ . ~~The Letter had and has~~ **If we again fail to comply with the Minimum Bid Price Rule, we will** ~~no~~ **not** ~~immediate effect on our continued~~ **be able to again complete a reverse stock split in compliance with applicable Nasdaq rules in the near term. If we are unable to comply with a** listing ~~on~~ **requirement of** The Nasdaq Capital Market ~~. Under Nasdaq Listing Rule 5810 (c) (3) (A)~~ , **including** ~~we have a 180- calendar day period, or until July 3, 2024 (the Compliance Date), to regain compliance with~~ the Minimum Bid Price Rule **, shares of** ~~. The Minimum Bid Price Rule will be met if~~ our Common Stock **would** ~~has a minimum closing bid price of at least $ 1. 00 per share for a minimum of 10 consecutive business days during the 180- calendar day period, unless Nasdaq exercises its discretion to extend such 10 - day period. If we do not regain compliance by the Compliance Date, we may be eligible for an additional 180- calendar day period, subject to satisfying the conditions in the applicable Nasdaq Listing Rules. If, before the Compliance Date, our Common Stock has a closing bid price of $ 0. 10 per share or less for ten consecutive trading days, the Staff (as defined below) will issue a Staff Delisting Determination under Nasdaq Listing Rule 5810 with respect to our Common Stock. On January 29, 2024, we filed an amendment to our Charter to implement the January 2024 Reverse Stock Split to attempt to regain compliance with the Minimum Bid Price Rule. Nasdaq subsequently reported that our Common Stock had a closing bid price above $ 1. 00 per share for 10 consecutive trading days during the 180- day period, but Nasdaq exercised its discretion to extend the 10- day period and did not deem that we regained compliance with the Minimum Bid Price Rule. There can be no assurance that we will be able to regain compliance or that the bid price of our Common Stock will remain above the minimum $ 1. 00 bid price required for any post- split Nasdaq monitoring period or otherwise. We will~~ likely ~~need to effect an additional reverse stock split of our Common Stock in an effort to regain compliance with the Minimum Bid Price Rule, but there can be no assurance that such a split may be approved or completed. On November 22, 2023, we received a letter from the Listing Qualifications Department (the Staff) of The Nasdaq Stock Market LLC (Nasdaq) notifying us that we are not in compliance with the minimum stockholders' equity requirement for continued listing on The Nasdaq Capital Market (the Notice) based on the information provided in our Quarterly Report on Form 10- Q for the quarter ended September 30, 2023. Nasdaq Listing Rule 5550 (b) (1) requires that companies listed on The Nasdaq Capital Market with a market value of listed securities of less than $ 35. 0 million and annual net income of less than $ 0. 5 million maintain stockholders' equity of at least $ 2. 5 million (the Stockholders' Equity Requirement). In accordance with Nasdaq rules, we were provided until January 8, 2024 to submit a plan to regain compliance with the Stockholders' Equity Requirement (the Compliance Plan). The Notice has no immediate effect on our continued listing on The Nasdaq Capital Market, subject to our compliance with other continued listing requirements. On January 22, 2024, the Staff granted us an extension until May 20, 2024 to regain compliance with the Stockholders' Equity Requirement. Per the Staff' s January 22, 2024 letter, we must complete an equity offering to raise gross proceeds of at least $ 6. 0 million (the Equity Offering) and furnish to the Staff and Nasdaq evidence of compliance with the Stockholders' Equity Requirement by filing a publicly available report prior to May 24, 2024. While we have completed the Equity Offering, the proceeds were insufficient for us to regain compliance with the Stockholders' Equity Requirement such that we will need to raise substantial additional funds in the near term. If we fail to evidence compliance with the Stockholders' Equity Requirement in our Quarterly Report for the quarter ending June 30, 2024, we may~~ be delisted ~~. There can be no assurance that we will be able to regain compliance~~ . If our Common Stock is delisted by Nasdaq, our Common Stock may be eligible to trade on the OTC Markets or another over- the- counter market, but a delisting, threatened delisting or trading on these markets would likely result in it being more difficult for us to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, our Common Stock. In addition, there can be no assurance that our Common Stock would be eligible for trading on any such alternative exchange or markets. Unless our Common Stock is listed on a national securities exchange, such as The Nasdaq Capital Market, our Common Stock may also be subject to the regulations and restrictions regarding trading in " penny stocks, " which are those securities trading for less than $ 5. 00 per share, and that are not otherwise exempted from the definition of a penny stock under other exemptions provided for in the applicable regulations. These requirements and regulations could severely limit the liquidity of securities in the secondary market because fewer brokers or dealers would likely to be willing to undertake related compliance activities. If our Common Stock is not listed on a national securities exchange, the rules and restrictions regarding penny stock transactions may limit an investor' s ability to sell to a third - party and our trading activity in the secondary market may be reduced ~~. Further, our failure to maintain compliance with applicable Nasdaq listing requirements will also cause us to fail to meet the equity conditions for us to require the exercise the Series T Warrants and may result in our being liable for penalties in our various investor agreements~~ . Any of these or the above circumstances could adversely affect our business, results of operation, prospects and the value of shares of our Common Stock. A delisting for this reason or any other reason could materially affect our ability to raise capital, adversely affect our business and the price of our Common Stock. ~~The January 2024 Reverse Stock Split may have caused our stock price to decline relative to its value before the split and decrease the liquidity of shares of our Common Stock.~~ We legally effected the ~~January~~ **February** ~~2024~~ **2025** Reverse Stock Split on ~~January 29~~ **February 21** , ~~2024~~ **2025** and on ~~January 30~~ **February 24** , ~~2024~~ **2025** , our Common Stock began trading on a post- split basis. ~~There is no~~ **It cannot be** ~~assurance~~ --- **assured** that the ~~January~~ **February** ~~2024~~ **2025** Reverse Stock Split ~~has~~ **will result**

in any sustained proportionate increase in the market price of our Common Stock, which is dependent upon many factors, including our business and financial performance, general market conditions, and prospects for future success, which are unrelated to the number of shares of our Common Stock outstanding. It is not ~~and will not~~ **uncommon for the market price of a company' s common stock to decline in the period following a reverse stock split. The February 2025 Reverse Stock Split may have** ~~cause~~ **caused a** ~~an actual~~ decline in the value of our outstanding Common Stock. ~~The~~ **Additionally, the** trading volume of our shares following the ~~April~~ **reverse stock splits completed since** 2023 ~~Reverse Stock Split~~ has varied, and shares of our Common Stock ~~may~~ have been less liquid as a result of ~~the~~ **these** ~~April 2023 Reverse~~ **reverse** ~~Stock~~ **stock** ~~Split~~ **splits** . ~~The~~ **It is likely that the** liquidity of the shares of our Common Stock **was** ~~may be~~ affected adversely by the ~~January~~ **February** ~~2024~~ **2025** Reverse Stock Split given the reduced number of shares outstanding following the ~~January~~ **February** ~~2024~~ **2025** Reverse Stock Split **. There can be no assurance that the liquidity of our Common Stock will increase** , especially if the market price of our Common Stock does not increase ~~as a result of the January 2024 Reverse Stock Split~~ . **Following a** ~~In addition, the January 2024 Reverse Stock Split may have increased the number of stockholders who own odd lots (less than 100 shares) of our Common Stock, creating the potential for such stockholders to experience an increase in the cost of selling their shares and greater difficulty effecting such sales. We expect to need to complete an additional~~ reverse stock split **, the resulting market price** of our Common Stock ~~given~~ **may not attract new investors, including institutional investors, and may not satisfy the investing requirements of those investors. Consequently, the trading liquidity of our Common Stock may not improve. Although we believe** that ~~our current bid~~ **a higher market** price ~~does not comply with the Minimum Bid Price Rule~~ **of our Common Stock may help generate greater or broader investor interest** , ~~but~~ there can be no assurance that ~~such a split will be approved or completed. Following~~ a reverse stock split, ~~the resulting market price of our Common Stock may not attract new investors,~~ including ~~institutional investors, and may not satisfy the investing requirements of those~~ -- **the recently completed February** ~~investors. Consequently, the trading liquidity of our Common Stock may not improve. Although we believe that a higher market price of our Common Stock may help generate greater or broader investor interest, there can be no assurance that a reverse stock split, including the January 2024~~ **2025** Reverse Stock Split, will result in a share price that will attract new investors, including institutional investors. In addition, there can be no assurance that the market price of our Common Stock will satisfy **or continue to satisfy** the investing requirements of those investors. As a result, the trading liquidity of our Common Stock may not necessarily improve. The primary intent for the ~~January~~ **February** ~~2024~~ **2025** Reverse Stock Split was to increase the price of our Common Stock in order to help us meet the Minimum Bid Price Rule pursuant to Nasdaq listing requirements ~~, but the January 2024 Reverse Stock Split did not result in the price of our Common Stock meeting the Minimum Bid Price Rule. As a result, we will likely need to effect an additional reverse stock split of our Common Stock, which may not be approved or completed~~ . It cannot be assured that a reverse stock split **, including the February 2025 Reverse Stock Split,** will result in any sustained proportionate increase in the market price of our Common Stock, which is dependent upon many factors, including our business and financial performance, general market conditions, and prospects for future success, which are unrelated to the number of shares of our Common Stock outstanding. ~~In fact, the January 2024 Reverse Stock Split did not result in a sustained proportionate increase in the market price of our Common Stock, in part due to the dilutive effects of the Equity Offering and subsequent warrant exercises.~~ It is not uncommon for the market price of a company' s common stock to decline in the period following a reverse stock split ~~or~~ **such as occurred** following ~~an offering~~ **the reverse stock splits completed since 2023** . Changes in tax law could adversely affect our business. The rules dealing with U. S. federal, state and local income taxation are constantly under review by the Internal Revenue Service **(IRS)** , the U. S. Treasury Department, and other governmental bodies. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our Common Stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition, or results of operations. An active trading market for our Common Stock may not develop and our stockholders may not be able to resell their shares of Common Stock for a profit, if at all. An active trading market for our shares of Common Stock may never develop or be sustained. If an active market for our Common Stock does not develop or is not sustained, it may be difficult for our stockholders to sell their shares at an attractive price or at all. If equity research analysts do not publish research or reports, **continue to publish reports** or publish unfavorable research or reports, about us, our business, or our market, our stock price and trading volume could decline. The trading market for our Common Stock will be influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts ~~have not currently elected and~~ may not elect to provide research coverage of our Common Stock **or may elect to discontinue coverage of our Common Stock** , and such lack of research coverage may adversely affect the market price of our Common Stock. **We do** ~~In the event we have equity research analyst coverage, we will~~ not have any control over the analysts, or the content and opinions included in their reports. The price of our Common Stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research **or discontinue coverage of our Common Stock** . If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our Common Stock could decrease, which in turn could cause our stock price or trading volume to decline. We may become a defendant in one or more stockholder derivative or class- action litigations, and any such future lawsuit may adversely affect our business, financial condition, results of operations and cash flows. We and certain of our officers and directors may become defendants in one or more future stockholder derivative actions or other class- action lawsuits. These lawsuits would divert our management' s attention and resources from our ordinary business operations, and we would likely incur significant expenses associated with their defense (including, without limitation, substantial attorneys' fees and other fees of professional advisors and potential obligations to indemnify current and former officers and directors who are or may become parties to such actions). If these lawsuits do arise, we may be required to pay material damages, consent to injunctions on future conduct and / or suffer other penalties, remedies or sanctions. In addition, any such future stockholder lawsuits could adversely impact our reputation,

our ability to continue to develop our product candidates, thereby harming our ability to generate revenue. Accordingly, the ultimate resolution of these matters could have a material adverse effect on our business, financial condition, results of operation and cash flow and, consequently, could negatively impact the trading price of our Common Stock. Our ~~charter~~ **amended and restated certificate of incorporation** documents and Delaware law may inhibit a takeover that stockholders consider favorable. Certain provisions of our amended and restated certificate of incorporation ~~(Charter)~~ and our amended and restated bylaws ~~(the Bylaws)~~ and applicable provisions of Delaware law may delay or discourage transactions involving an actual or potential change in control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. The provisions in our ~~Charter~~ **amended** and **restated certificate of incorporation and amended and restated** ~~Bylaws~~ **bylaws** : • limit who may call stockholder meetings; • do not provide for cumulative voting rights; • provide that all vacancies may be filled only by the affirmative vote of a majority of directors then in office, even if less than a quorum; • provide that the Court of Chancery of the State of Delaware will be the exclusive forum for certain legal claims; and • provide that the federal district courts of the United States of American will be the exclusive forum for legal claims under the Securities Act. In addition, Section 203 of the **DGCL** ~~Delaware General Corporation Law~~ may limit our ability to engage in any business combination with a person who beneficially owns 15 % or more of our outstanding voting stock unless certain conditions are satisfied. This restriction lasts for a period of three years following the share acquisition. These provisions may have the effect of entrenching our management team and may deprive stockholders' of the opportunity to sell their shares to potential acquirers at a premium over prevailing prices. This potential inability to obtain a control premium could reduce the price of our common stock. Furthermore, our ~~Charter~~ **amended and restated certificate of incorporation** specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to our or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our ~~Charter or~~ **amended and restated certificate of incorporation** ~~our~~ **or our amended and restated** ~~Bylaws~~ **bylaws** , or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. We believe these provisions provide increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi- forum litigation. However, these provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in the ~~Charter~~ **amended and restated certificate of incorporation** to be inapplicable or unenforceable in such action. This choice of forum provision does not preclude or contract the scope of exclusive federal jurisdiction for any actions brought under the Exchange Act. 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. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction, and we do not intend for the exclusive forum provision to apply to Exchange Act claims. Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, there is uncertainty as to whether a court would enforce such a forum selection provision as written in connection with claims arising under the Securities Act. Additionally, this choice of forum provision will not apply to claims as to which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. The choice of forum provision in the ~~Charter~~ **amended and restated certificate of incorporation** does not have the effect of causing our stockholders to have waived our obligation to comply with the federal securities laws and the rules and regulations thereunder.