Risk Factors Comparison 2025-02-19 to 2024-02-15 Form: 10-K

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Risks Related to Our Business and our Industry: • the significant operating losses we have incurred and expect to incur for the foreseeable future; • our ability to obtain the capital necessary to fund our operations; • we do not have any products that are approved for commercial sale and do not expect to generate any revenues from product sales for the foreseeable future, if ever; • our dependence on the success of our MN- 166 (ibudilast) and MN- 001 (tipelukast) product candidates and uncertainty that these product candidates will receive regulatory approval or be successfully commercialized; • the complexity and uncertainty relating to progressing product candidates through the various stages of clinical trials and obtaining regulatory approval; • our attempts to develop MN- 001 (tipelukast) in NASH ~~,~~ **(as defined below) and** NAFLD ~~, and IPF~~ **(as defined below)** may detract from our efforts to develop other product candidates; • the complexity, high cost and uncertainty of obtaining regulatory approval; • the stringent regulation of our product candidates; • future development and regulatory difficulties even if we are successful in receiving regulatory approval of one or more of our product candidates; • undesirable side effects of any product candidate experienced during clinical trials could delay or prevent regulatory approval or commercialization or limit its commercial potential; • delays in the commencement or completion of clinical trials, or suspension or termination of our clinical trials; • the loss of any rights to develop and market any of our product candidates; • the impact of **health epidemics** ~~the COVID- 19 pandemic or any other illness or communicable disease,~~ or any other public health crisis on our business **and operations** ; • our dependence on strategic collaborations with third parties to develop and commercialize product candidates; • our reliance on third parties to conduct our clinical trials; • our reliance on third party manufacturers to produce our product candidates; • our, or our third ~~-~~party manufacturer' s ability to manufacture our product candidates in commercial quantities; • the commercial availability of materials necessary to manufacture our product candidates; • the acceptance among physicians, patients and the medical community of our product candidates; • the ability of users of our products to obtain adequate coverage of and reimbursement for our products from government and other third party payers; • our ability to retain, motivate and attract key personnel; • our ability to establish sales, marketing and distribution capabilities; • health care reform measures could adversely affect our business; • the impact of any product liability lawsuits against us; • the impact of fluctuations in our results of operations; • the cost of and management attention required to operate as a public company; • information technology systems failures, network disruptions, breaches in data security and computer crime and cyber- attacks; **and** • the complexity of operating our business and marketing our products internationally ~~;~~ **.** Risks Related to Our Intellectual Property: • our ability to compete depends on the adequate protection of our proprietary rights; • the potential disclosure of our trade secrets and other proprietary information; **and** • the costs and uncertainties of any dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others, including trade secrets ~~;~~ **.** Risks Related to the Securities Markets and Investments in Our Common Stock **:** • volatility in our stock price; • the potential delisting of our common stock on the Nasdaq Global Market or the Standard Market of the Tokyo Stock Exchange; • the possibility of substantial dilution to our existing stockholders and / or the decline in price of our common stock if we were to sell additional shares of our common stock, including under our existing at- the- market issuance sales agreement; • the cost of and management distraction if we were to face securities class action litigation; and • the anti- takeover provisions in our charter documents and under Delaware law may make it difficult for third parties to acquire us or remove and replace our directors and management. Item 1. Business Overview We are a biopharmaceutical company focused on developing novel therapeutics for the treatment of serious diseases with unmet medical needs and a commercial focus on the United States **(U. S.)** market. Our current strategy is to focus our development activities on MN- 166 (ibudilast) for neurological and other disorders such as progressive multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), chemotherapy- induced peripheral neuropathy, degenerative cervical myelopathy, glioblastoma, substance dependence and addiction (e. g., methamphetamine dependence, opioid dependence, and alcohol dependence), prevention of acute respiratory distress syndrome (ARDS), and Long COVID, and MN- 001 (tipelukast) for fibrotic and other ~~diseases~~ **metabolic disorders** such as nonalcoholic fatty liver disease (NAFLD) and **hypertriglycedemia** ~~idiopathic pulmonary fibrosis (IPF). Our pipeline also includes MN- 221 (bedoradrine) for the treatment of acute exacerbation of asthma and MN- 029 (denibulin) for solid tumor cancers. MN- 166 (ibudilast) is in development for several different neurological diseases and other diseases as described below~~ . Progressive Multiple Sclerosis: We completed a Phase 2b clinical trial of MN- 166 (ibudilast) for the treatment of relapsing ~~multiple sclerosis (~~ MS ~~)~~ , in which positive safety and neuroprotective efficacy indicators were observed. The data from this trial indicated that MN- 166 (ibudilast) may have potential in the treatment of progressive MS. We partnered with investigators on a Phase 2b clinical trial of MN- 166 (ibudilast) in primary progressive and secondary progressive MS which was conducted by NeuroNEXT and funded by the National Institute of Health' s (NIH) National Institute of Neurological Diseases and Stroke (NINDS). This progressive MS trial, known as SPRINT- MS, completed randomization of 255 subjects in 2015, which exceeded the goal of 250 subjects that were planned for participation. In October 2017, we announced the presentation of positive top- line results from the SPRINT- MS Phase 2b clinical trial of MN- 166 (ibudilast) in progressive MS. The trial achieved both primary endpoints of whole brain atrophy and safety and tolerability. MN- 166 (ibudilast) demonstrated a statistically significant 48 % reduction in the rate of progression of whole brain atrophy compared to placebo (p = 0. 04) as measured by **magnetic resonance imaging (** MRI **)** analysis using brain parenchymal fraction (BPF) and there was not an increased rate of serious adverse events in the MN- 166 (ibudilast) group compared to the placebo group. In February 2018, we announced the presentation of positive clinical efficacy trends from this trial regarding the important secondary endpoint of confirmed disability progression. MN- 166 (ibudilast) demonstrated a 26 % reduction in the risk of

confirmed disability progression compared to placebo (hazard ratio = 0. 74), as measured by ~~EDSS (~~Expanded Disability Status Scale **(EDSS**). Results of the SPRINT- MS Phase 2b clinical trial of MN- 166 (ibudilast) in progressive MS were published in the New England Journal of Medicine in August 2018. In April 2019, we announced results from a subgroup analysis of the SPRINT- MS Phase 2b trial of MN- 166 (ibudilast) in progressive MS which showed that the trends for reduction in the risk of confirmed disability progression were highest for the subgroup of subjects with ~~Secondary~~ **secondary** ~~Progressive~~ **progressive** MS without ~~Relapse~~ **relapse** , in which MN- 166 (ibudilast) demonstrated a 46 % risk reduction compared to placebo. Additional data from the completed SPRINT- MS Phase 2b trial of MN- 166 (ibudilast) in progressive MS was presented in May 2019 at the American Academy of Neurology (AAN) 71st Annual Meeting in Philadelphia, Pennsylvania. In November 2020, we announced that positive Optical Coherence Tomography (OCT) results from the SPRINT- MS Phase 2b trial of MN- 166 (ibudilast) in progressive MS were published in Multiple Sclerosis Journal. In July 2021, we received a Notice of Allowance from the U. S. Patent and Trademark Office **(USPTO)** for a new patent which covers MN- 166 (ibudilast) for the treatment of an ophthalmic disease / disorder or injury associated with a neurodegenerative disease / disorder or a neuro- ophthalmologic disorder. The ~~United States Food and Drug Administration (~~FDA ~~)~~ has granted Fast Track designation for the development of MN- 166 (ibudilast) for the treatment of patients with progressive MS. Amyotrophic Lateral Sclerosis ~~(ALS)~~ : We initiated a clinical trial of MN- 166 (ibudilast) in amyotrophic lateral sclerosis (ALS) in the second half of 2014, and this trial was completed during the second half of 2017. In December 2017, we announced positive top- line results from this trial. The trial achieved the primary endpoint of safety and tolerability. In addition, there was a higher rate of responders on the Amyotrophic Lateral Sclerosis Functional Rating Scale- Revised (ALSFRS- R) total score, a measure of functional activity, in the MN- 166 (ibudilast) group compared to the placebo group. In September 2018, we received feedback from the FDA regarding our clinical development plan for MN- 166 (ibudilast) in ALS. In January 2019, we received a Notice of Allowance from the **USPTO** ~~U. S. Patent and Trademark Office~~ for a new patent which covers the combination of MN- 166 (ibudilast) and riluzole for the treatment of ALS and other neurodegenerative diseases. In April 2019, we announced that the FDA completed its review of the protocol and determined that we may proceed with a Phase 2b / 3 clinical trial of MN- 166 (ibudilast) in ALS. In June 2019, we announced a kick- off meeting for the Phase 2b / 3 clinical trial of MN- 166 (ibudilast) in ALS. In December 2019, we announced that additional analyses of the completed clinical trial of MN- 166 (ibudilast) in ALS was presented at the 30th International Symposium on ~~ALS / MND (~~amyotrophic lateral sclerosis / motor ~~neurone~~ **neuron** disease **(ALS / MND**) in Perth, Australia. In December 2021, we announced that a poster with an overview of our ongoing Phase 2b / 3 clinical trial of MN- 166 (ibudilast) in ALS was presented at the 32nd International Symposium on ALS / MND **. In December 2024, a study update and interim analysis of phase 2 / 3 clinical data of MN- 166 (ibudilast) in the COMBAT- ALS trial was presented at the 35th international symposium on ALS / MND at Montreal, Canada** . The FDA has granted Fast Track designation to MN- 166 (ibudilast) for the treatment of ALS as well as Orphan- Drug designation for the treatment of ALS, which will provide seven years of marketing exclusivity if it is approved for ALS. The European Commission also granted Orphan Medicinal Product Designation for MN- 166 (ibudilast) for the treatment of ALS. Substance Dependence and Addiction: In ~~the area of addiction, the National Institute on Drug Abuse (NIDA) funded a Phase 2 clinical trial of MN- 166 (ibudilast) for the treatment of methamphetamine addiction. In collaboration with the University of California, Los Angeles (UCLA), this clinical trial commenced in 2013 and enrollment was completed in September 2017. In March 2018, we announced that this trial did not meet the primary endpoint of methamphetamine abstinence confirmed via urine drug screens during the final two weeks of treatment. In~~ November 2017, we announced a collaboration with Oregon Health & Science University to initiate a biomarker study for evaluating MN- 166 (ibudilast) in methamphetamine use disorder and this trial is ongoing. Investigators at Columbia University and the New York State Psychiatric Institute (NYSPI) previously completed a Phase 1b / 2a clinical trial of MN- 166 (ibudilast) in opioid withdrawal that was funded by **National Institute Drug Abuse (** NIDA **)** . Investigators at Columbia University and the NYSPI also conducted a NIDA- funded, Phase 2a clinical trial to evaluate the efficacy of MN- 166 (ibudilast) in the treatment of patients addicted to prescription opioids or heroin. In March 2016, we announced that positive findings from the results of this completed study in opioid dependence were presented at the Behavior, Biology and Chemistry: Translational Research in Addiction Meeting. Researchers at **University of California, Los Angeles (** UCLA **)** were granted approval and funding by the National Institute on Alcoholism and Alcohol Abuse (NIAAA) for a clinical trial to evaluate MN- 166 (ibudilast) for the treatment of alcohol dependence. This clinical trial has been completed and results were presented at the American College of Neuropsychopharmacology (ACNP)' s 54th Annual Meeting in December 2015. In May 2018, we announced a new NIDA- funded clinical trial of MN- 166 (ibudilast) in alcohol dependence and withdrawal in collaboration with researchers at UCLA. This clinical trial has been completed and positive findings were presented at the American Psychological Association 2020 Annual Convention which was held online in August 2020. Results from this clinical trial were published in June 2021 in Nature' s Translational Psychiatry. In August 2018, we announced a new NIAAA- funded Phase 2b clinical trial of MN- 166 (ibudilast) to evaluate heavy drinking days in subjects with alcohol dependence in collaboration with researchers at UCLA and this trial has been completed. In February 2022, we announced that MN- 166 (ibudilast) was discussed as one of the promising pharmacological agents for the treatment of alcohol use disorder in the journal Drugs. In April 2022, we announced that a secondary analysis of a Phase 2 clinical trial of MN- 166 (ibudilast) in alcohol use disorder was published in the journal Alcoholism: Clinical and Experimental Research. In December 2022, we announced that positive results from a secondary analysis of a Phase 2 trial of MN- 166 (ibudilast) in alcohol use disorder were published in The American Journal of Drug and Alcohol Abuse. In January 2023, we announced that the Phase 2b clinical trial of MN- 166 (ibudilast) for the treatment of alcohol use disorder had completed enrollment. In June 2023, we announced results of the Phase 2b clinical trial of MN- 166 (ibudilast) in alcohol use disorder which were presented at the 46th Annual Research Society on Alcoholism (RSA) Scientific Meeting. Chemotherapy- Induced Peripheral Neuropathy: In March 2018, we announced plans to initiate a clinical trial to evaluate MN- 166 (ibudilast) as a treatment for prevention of chemotherapy- induced peripheral neuropathy (CIPN) which was

funded by the University of Sydney Concord Cancer Centre in Australia. In September 2020, we announced that positive clinical findings from this clinical trial were published in Cancer Chemotherapy and Pharmacology. In October 2020, we announced plans to initiate a multi- center, placebo- controlled, randomized Phase 2b trial to evaluate MN- 166 (ibudilast) in CIPN, which is funded by the Australasian Gastro- Intestinal Trials Group (AGITG), and this trial is ongoing. Degenerative Cervical Myelopathy: In August 2018, we announced plans to initiate a clinical trial of MN- 166 (ibudilast) in degenerative cervical myelopathy (DCM) in collaboration with the University of Cambridge. The trial is funded by a grant from the National Institute for Health Research (NIHR) in the United Kingdom (UK). In May 2019, we announced our participation at the Kick- off Meeting for the Phase 3 clinical trial in DCM, " REgeneration in CErvical DEgenerative Myelopathy (RECEDE Myelopathy) " in collaboration with University of Cambridge researchers. In February 2022, we announced that MN- 166 (ibudilast) was discussed as a potential beneficial pharmacological agent for the treatment of DCM in Global Spine Journal. Glioblastoma: We have initiated clinical development to evaluate MN- 166 (ibudilast) for the treatment of glioblastoma. In June 2017, we announced positive results from an animal model study that examined the potential clinical efficacy of MN- 166 (ibudilast) for the treatment of glioblastoma. These results were presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting. In May 2018, we announced that the Investigational New Drug Application (IND) for MN- 166 (ibudilast) for treatment of glioblastoma was accepted and opened with the FDA. In October 2018, we announced that the FDA granted orphan- drug designation to MN- 166 (ibudilast) as adjunctive therapy to temozolomide for the treatment of glioblastoma. In January 2019, we announced the initiation of enrollment in a clinical trial of MN- 166 (ibudilast) in combination with temozolomide for the treatment of glioblastoma at the Dana- Farber Cancer Institute in Boston. In February 2019, we announced that Scientific Reports published results from the animal model study evaluating MN- 166 (ibudilast) in glioblastoma. In June 2020, we announced that positive preclinical findings were published in Frontiers in Immunology regarding the prospect of MN- 166 (ibudilast) as an adjunctive treatment for glioblastoma. In August 2021, we announced completion of a safety review of Part 1 of the Phase 2 clinical trial of MN- 166 (ibudilast) in combination with temozolomide, which enrolled 15 subjects with recurrent glioblastoma. There were no concerning safety signals observed in Part 1 and there were no serious adverse events related to MN- 166 (ibudilast). Five out of 15 subjects completed cycle 6 without disease progression, i. e. 33 % of the subjects were progression- free at six months. In April 2022, we announced that data demonstrating that MN- 166 (ibudilast) prevents metastasis in a uveal melanoma (UM) animal model was published in the journal Molecular Cancer Research. In January 2023, we announced that the Phase 2 clinical trial evaluating MN- 166 (ibudilast) in combination with temozolomide in glioblastoma at the Dana- Farber Cancer Institute had completed enrollment. In February 2023, we announced the presentation of new data regarding a tumor tissue analysis from this clinical trial at the 20th Annual World Congress of ~~SBMT (~~Society for Brain Mapping and Therapeutics **(SBMT**). In November 2023, we announced new data and results of the Phase 2 clinical trial of MN- 166 (ibudilast) in glioblastoma patients at the 28th Annual Meeting of the Society for Neuro- Oncology (SNO). The presentation also included data from preclinical studies which evaluated the combination of MN- 166 (ibudilast) and anti- PD1 or anti- PD- L1 therapy in glioblastoma models **. In 2024, we presented new data and results of a Phase 1b / 2a Clinical Trial of MN- 166 (ibudilast) in glioblastoma at the ASCO Annual meeting 2024 held in Chicago, IL** . Prevention of ARDS in patients with COVID- 19: In March 2020, we announced plans to initiate development of MN- 166 (ibudilast) for severe pneumonia and ARDS based on positive results of a preclinical study in an animal model of ARDS. In April 2020, we announced plans to initiate a clinical trial of MN- 166 (ibudilast) for ARDS caused by COVID- 19. In July 2020, we announced that the IND for MN- 166 (ibudilast) for prevention of ARDS was accepted and opened with the FDA. We were also informed by the FDA that the proposed clinical investigation of MN- 166 (ibudilast) for the prevention of ARDS in patients with COVID- 19 may proceed. In April 2022, we announced that the Phase 2 clinical trial of MN- 166 (ibudilast) in hospitalized COVID- 19 patients at risk for developing ARDS had completed enrollment. In June 2022, we announced positive top- line results from this Phase 2 clinical trial. MN- 166 (ibudilast) demonstrated large improvements compared to placebo for all four clinical endpoints analyzed. The trial achieved statistical significance for one of the co- primary endpoints, the proportion of subjects free of respiratory failure. The trial also achieved statistical significance for the proportion of subjects discharged from the hospital. There were two deaths in the placebo group and no deaths in the MN- 166 (ibudilast) group. In July 2022, we announced the initiation of a first- in- human clinical study to evaluate a new parenteral (injectable) formulation of MN- 166 (ibudilast). In January 2023, we announced that this Phase I clinical trial of MN- 166 (ibudilast) 10 mg intravenous (IV) infusion in healthy volunteers was completed with a favorable safety profile and was well tolerated. Chlorine Gas- Induced Lung Injury: In March 2021, we announced a partnership with the Biomedical Advanced Research and Development Authority (BARDA), part of the Administration for Strategic Preparedness and Response (ASPR) in the U. S. Department of Health and Human Services, to develop MN- 166 (ibudilast) as a potential medical countermeasure (MCM) against chlorine gas- induced lung damage such as ARDS and acute lung injury (ALI). BARDA agreed to provide federal funding for proof- of- concept studies of MN- 166 (ibudilast) in preclinical models of chlorine gas- induced acute lung injury under Contract No. 75A50121C00022. In September 2023, we announced the results of the studies conducted under our contract with BARDA. The primary endpoint of the first nonclinical efficacy study was the pulmonary function measure PaO2 / FiO2, which is the ratio of arterial oxygen partial pressure to fractional inspired oxygen. In the pilot design single- dose treatment regimen, MN- 166 (ibudilast) high dose and the positive control rolipram were more efficacious than MN- 166 (ibudilast) low dose and the negative control until 12 hours after chlorine exposure but this did not yield statistically significant results for overall pulmonary function. In the multi- dose study, each treatment was given every 12 hours with a total of four doses after the chlorine gas challenge. Treatment with MN- 166 (ibudilast) high dose resulted in greater improvement ($p = 0.0001$) in the mean PaO2 / FiO2 ratio than MN- 166 (ibudilast) low dose, rolipram, and the negative control. MN- 166 (ibudilast) was well tolerated and no safety concerns were observed in the first nonclinical efficacy study. After multiple attempts by our subcontractor to establish the feasibility of the second chlorine- gas induced lung injury model, it was not deemed to be a feasible model to

evaluate a drug candidate and there are no evaluable efficacy results. Long COVID: In August 2022, we announced plans to participate in ~~RECLAIM (~~Recovering from COVID- 19 Lingering Symptoms Adaptive Integrative Medicine Trial **(RECLAIM trial**), a grant- funded, multi- center, randomized, clinical trial to evaluate MN- 166 (ibudilast) and other therapies for the treatment of Long COVID, the lingering symptoms of COVID- 19. In February 2023, we announced that Health Canada completed its review of the clinical trial application and granted authorization to commence the RECLAIM trial and this study is ongoing. MN- 001 (tipelukast) is in development for fibrotic and other ~~diseases~~ **metabolic disorders** as described below. Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (NAFLD): We announced positive results of MN- 001 (tipelukast) in two different NASH mouse models in 2014 and we opened the IND (Investigational New Drug) application for MN- 001 (tipelukast) for the treatment of NASH with the FDA in 2015. The FDA subsequently granted Fast Track designation to MN- 001 (tipelukast) for the treatment of patients with NASH with fibrosis. We then initiated a clinical trial to investigate MN- 001 (tipelukast) for the treatment of hypertriglyceridemia in NASH and NAFLD patients. In April 2018, we announced that we would terminate this trial early after positive results from an interim analysis in which MN- 001 (tipelukast) significantly reduced mean serum triglycerides, a primary endpoint. This data was presented at the International Liver Congress 2018, the 53rd annual meeting of the European Association for the Study of the Liver (EASL) in Paris, France in April 2018. In November 2020, we announced positive results of in- vitro and in- vivo studies that evaluated MN- 001 (tipelukast) for its anti-liver fibrotic effect in human hepatic stellate cells (HSCs) and in an acute liver injury model at the annual meeting of the American Association for the Study of Liver Diseases (AASLD). In November 2021, we announced new findings from a study that investigated the mechanism by which MN- 001 (tipelukast) alters triglyceride metabolism in hepatocytes at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). In April 2022, we announced that the FDA completed its review of a proposed Phase 2 clinical trial to evaluate MN- 001 (tipelukast) for the treatment of patients with NAFLD, type 2 diabetes mellitus, and hypertriglyceridemia and the study may proceed. In July 2022, we announced the initiation of a Phase 2 clinical trial to evaluate MN- 001 (tipelukast) for the treatment of patients with NAFLD, type 2 diabetes mellitus, and hypertriglyceridemia. In December 2022, we announced the presentation of positive results from a subgroup analysis of the completed Phase 2 clinical trial which evaluated MN- 001 (tipelukast) in participants with NAFLD and hypertriglyceridemia (HTG) at the International Diabetes Federation (IDF) World Diabetes Congress 2022. ~~Idiopathic Pulmonary Fibrosis (IPF): In~~ **May** ~~2014~~ **2024** , we **presented** ~~announced positive results of MN- 001 (tipelukast) in a mouse model of pulmonary fibrosis. The FDA subsequently granted Orphan- Drug designation to MN- 001 (tipelukast) for treatment of IPF which will provide seven years of marketing exclusivity if MN- 001 (tipelukast) is approved for IPF. The FDA granted Fast Track designation to MN- 001 (tipelukast) for the treatment of patients with IPF in September 2015. We then initiated a Phase 2 clinical trial of MN- 001 (tipelukast) to treat IPF and we announced results of this trial in August 2021. Although there were no clinically meaningful trends in favor of MN- 001 (tipelukast) for the majority of the clinical outcome measures in this small study, there were no worsening IPF events (acute IPF exacerbation or hospitalization due to respiratory symptoms) in the MN-001 (tipelukast) group compared to one worsening IPF event in the placebo group. MN- 001 (tipelukast) demonstrated a substantial reduction in LOXL2, a biomarker for IPF, whereas LOXL2 increased in the placebo group. MN- 001 (tipelukast) was safe and well tolerated. We completed a Phase 2 clinical trial of MN- 221 (bedoradrine) for the treatment of acute exacerbations of asthma treated in the emergency room and conducted~~ an **update** ~~End-~~ of **ongoing** ~~- Phase 2 meeting with the FDA in October 2012. In that meeting, the FDA identified the risk / benefit profile of MN- 221 (bedoradrine) as a focal point for further development and advised that a clinical outcome, such as a reduction in hospitalizations, would need to be a primary endpoint in a pivotal trial. We believe the appropriate clinical development for MN- 221 (bedoradrine) would involve conducting dose regimen and acute exacerbations of asthma~~ trial design **at the 92nd European Atherosclerosis Society (EAS) 2024 Congress** ~~optimization studies prior to commencing pivotal trials. We plan to identify a partner for financial support before further clinical development is commenced~~ . We acquired licenses to MN- 166 (ibudilast) ~~,~~ **and** MN- 001 (tipelukast ~~), MN- 221 (bedoradrine), and MN- 029 (denibulin~~) for the development of these product candidates ~~. The MN- 221 (bedoradrine) license agreement was terminated in October 2022~~ . We have pursued development of these product candidates in various indications including prevention of acute respiratory distress syndrome, Long COVID, progressive MS, ALS, chemotherapy- induced peripheral neuropathy, degenerative cervical myelopathy, glioblastoma, various addictions, NASH and NAFLD ~~, IPF, acute exacerbations of asthma, and solid tumor cancers~~ . Our Strategy Our goal is to build a sustainable biopharmaceutical business through the successful development of differentiated products for the treatment of serious diseases with unmet medical needs in high- value therapeutic areas. Key elements of our strategy are as follows: • Pursue the development of MN- 166 (ibudilast) for multiple potential indications with the support of non- dilutive financings. We intend to advance our diverse MN- 166 (ibudilast) program through a combination of investigator- sponsored clinical trials, trials funded through government grants or other grants, and trials funded by us. We intend to pursue additional strategic alliances to help support further clinical development of MN- 166 (ibudilast). • Pursue the development of MN- 001 (tipelukast) for fibrotic and other ~~diseases~~ **metabolic disorders** . We intend to advance development of MN- 001 (tipelukast) through a variety of means, which may include investigator- sponsored trials with or without grant funding as well as trials funded by us. • Consider strategic partnerships with one or more leading pharmaceutical companies to complete product development and successfully commercialize our products. We develop and maintain relationships with pharmaceutical companies that are therapeutic category leaders. We intend to discuss strategic alliances with leading pharmaceutical companies who seek product candidates, such as MN- 166 (ibudilast) ~~,~~ **and** MN- 001 (tipelukast ~~), MN- 221 (bedoradrine), and MN- 029 (denibulin~~), which could support our clinical development and product commercialization. Our Product Candidates and Programs Our product development programs address diseases that we believe are not well served by currently available therapies and represent significant commercial opportunities. We believe that we have product candidates that offer innovative therapeutic approaches that may provide significant advantages relative to current therapies. Our product acquisitions have focused primarily on

product candidates with significant preclinical and early clinical testing data that have been developed by the licensors outside of the United States. We utilize the existing data in preparing IND Applications or their foreign equivalents, and in designing and implementing additional preclinical or clinical trials to advance the development programs in the United States or abroad. Following are the details of our product development programs: MN- 166 (ibudilast) is a novel, first- in- class, oral, anti- inflammatory and neuroprotective agent. MN- 166 (ibudilast) inhibits macrophage migration inhibitory factor (MIF) and certain phosphodiesterases (PDEs). MN- 166 (ibudilast) also attenuates activated glia cells, which play a major role in certain neurological conditions. While it has been in use for more than 20 years in Japan and Korea for the treatment of asthma and post- stroke dizziness, we are developing MN- 166 (ibudilast) for the treatment of progressive MS, ALS, chemotherapy- induced peripheral neuropathy, degenerative cervical myelopathy, glioblastoma, substance dependence, prevention of acute respiratory distress syndrome, and Long COVID. We licensed MN- 166 (ibudilast) from Kyorin Pharmaceuticals (Kyorin) in 2004. The FDA has granted Fast Track designations to MN- 166 (ibudilast) for three separate indications: the treatment of progressive MS, the treatment of ALS, and the treatment of methamphetamine dependence. Fast track designation is a process designed to facilitate the development and expedite the review of drugs that are intended to treat serious diseases and have the potential to fill an unmet medical need. An important feature of the FDA' s Fast Track program is that it emphasizes early and frequent communication between the FDA and the sponsor throughout the entire drug development and review process to improve the efficiency of product development. Accordingly, Fast Track status can potentially lead to a shortened timeline to ultimate drug approval. The FDA has granted Orphan- Drug designation to MN- 166 (ibudilast) for the treatment of ALS, which will provide seven years of marketing exclusivity if it is approved for ALS in the U. S. The European Commission also granted Orphan Medicinal Product Designation for MN- 166 (ibudilast) for the treatment of ALS which offers potential benefits including ten years of marketing exclusivity if it is approved for ALS in Europe. The FDA has also granted Orphan- Drug designation to MN- 166 (ibudilast) as adjunctive therapy to temozolomide for the treatment of glioblastoma. We have filed patent applications for multiple uses of MN- 166 (ibudilast) for the treatment of neurological conditions. Some of the patent estate has received allowance in the United States and foreign countries. For example, we have been granted separate U. S. patents that cover the use of MN- 166 (ibudilast) for the treatment of progressive MS, for the treatment of ALS, for the treatment of glioblastoma, for the treatment of drug addiction or dependence, and for the treatment of neuropathic pain. Progressive Multiple Sclerosis: MS is a complex disease with predominantly unknown etiology and affects approximately 2. 8 million people worldwide, according to the National Multiple Sclerosis Society **(** ~~, or~~ NMSS **)** . Also, according to NMSS, approximately 85 percent of people with MS are initially diagnosed with relapsing- remitting MS **(** ~~, or~~ RRMS ~~,~~ **)** and some people who are initially diagnosed with RRMS will eventually transition to secondary progressive MS **(** ~~, or~~ SPMS **)** . About 15 percent of people with MS are diagnosed with primary progressive MS **(** ~~, or~~ PPMS **)** . There is only one approved drug for PPMS and it is administered by intravenous infusion. Although several drugs have been approved for SPMS with relapses, there are no approved drugs generally considered safe and efficacious for SPMS in the absence of relapses. There is a significant medical need for a safe, effective, and conveniently administered therapy for patients with PPMS and SPMS and the unmet medical need is highest in patients with SPMS without relapses. MN- 166 (ibudilast) may meet these needs. Based on promising results from a Phase 2 trial in relapsing MS completed in 2008, investigators from NeuroNEXT, a NIH- funded Phase 2 clinical trial network, evaluated MN- 166 (ibudilast) in PPMS and SPMS patients in the United States. SPRINT- MS is the name of the Phase 2b, randomized, double- blind, placebo- controlled trial that evaluated the safety and tolerability of MN- 166 (ibudilast) (up to 100 mg / day) in PPMS and SPMS patients. Recruitment and enrollment at 28 medical centers in the United States commenced in late 2013 and randomization of 255 subjects was completed in June 2015. In October 2017, we announced the presentation of positive top- line results from the SPRINT- MS Phase 2b clinical trial of MN- 166 (ibudilast) in progressive MS. The trial achieved both primary endpoints of whole brain atrophy and safety and tolerability. MN- 166 (ibudilast) demonstrated a statistically significant 48 % reduction in the rate of progression of whole brain atrophy compared to placebo (p = 0. 04) as measured by MRI analysis using brain parenchymal fraction (BPF) and there was not an increased rate of serious adverse events in the MN- 166 (ibudilast) group compared to the placebo group. In February 2018, we announced the presentation of positive clinical efficacy trends from this trial regarding the important secondary endpoint of confirmed disability progression. MN- 166 (ibudilast) demonstrated a 26 % reduction in the risk of confirmed disability progression compared to placebo (hazard ratio = 0. 74), as measured by ~~EDSS (~~ Expanded Disability Status Scale **(EDSS**). Results of the SPRINT- MS Phase 2b clinical trial of MN- 166 (ibudilast) in progressive MS were published in the New England Journal of Medicine in August 2018. In April 2019, we announced results from a subgroup analysis of the SPRINT- MS Phase 2b trial of MN- 166 (ibudilast) in progressive MS. The purpose of the subgroup analysis was to provide information about which types of progressive MS subjects responded best to MN- 166 (ibudilast) treatment in terms of the clinically significant endpoint of the risk of confirmed disability progression compared to placebo, as measured by EDSS. The trends for reduction in the risk of confirmed disability progression were highest for the subgroup of subjects with ~~Secondary~~ **secondary** ~~Progressive~~ **progressive** MS without Relapse, in which MN- 166 (ibudilast) demonstrated a 46 % risk reduction compared to placebo as indicated by the hazard ratio of 0. 538. Additional data from the completed SPRINT- MS Phase 2b trial of MN- 166 (ibudilast) in progressive MS was presented in May 2019 at the American Academy of Neurology (AAN) 71st Annual Meeting in Philadelphia. In November 2020, we announced that positive Optical Coherence Tomography (OCT) results from the SPRINT- MS Phase 2b trial of MN- 166 (ibudilast) in progressive MS were published in Multiple Sclerosis Journal. OCT measures included macular volume ~~, pRNFL (~~ peripapillary retinal nerve fiber layer **(pRNFL**) thickness, and ganglion cell- inner plexiform (GCIP) layer thickness. All of these OCT measures showed less loss of retinal tissue for MN- 166 (ibudilast) compared to placebo. In July 2021, we received a Notice of Allowance from the **USPTO** ~~U. S. Patent and Trademark Office~~ for a new patent which covers MN- 166 (ibudilast) for the treatment of an ophthalmic disease / disorder or injury associated with a neurodegenerative disease / disorder or a neuro- ophthalmologic disorder. We were granted Fast Track designation from the FDA for MN- 166 (ibudilast) for the treatment of

progressive MS in 2016. Amyotrophic Lateral Sclerosis ~~(ALS)~~ : ALS, also known as Lou Gehrig' s disease, is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. The nerves lose the ability to trigger specific muscles, which causes the muscles to become weak. As a result, ALS affects voluntary movement and patients in the later stages of the disease may become totally paralyzed. Mean survival time of an ALS patient is two to five years. According to the ALS Association, there are at least 16, 000 ALS patients in the United States and approximately 5, 000 people in the United States are diagnosed with ALS each year. We have worked with Carolinas Neuromuscular / ALS- MDA Center at Carolinas HealthCare System Neurosciences Institute, which has conducted a clinical trial of MN- 166 (ibudilast) in ALS. The trial was a randomized, double- blind, placebo- controlled study which included a six- month treatment period followed by a six- month open- label extension. The study evaluated the safety and tolerability of MN- 166 (ibudilast) 60 mg / day versus placebo when administered in combination with riluzole in subjects with ALS, as well as several efficacy endpoints. Subject enrollment began in October 2014. In April 2016, we announced that interim efficacy data from a mid- study analysis of the clinical trial of MN- 166 (ibudilast) in ALS was presented at the ~~American Academy of Neurology (~~AAN ~~)~~ 68th Annual Meeting. In December 2017, we announced positive top- line results from the ALS trial at Carolinas Neuromuscular / ALS- MDA Center. The trial achieved the primary endpoint of safety and tolerability. In addition, there was a higher rate of responders on the ALSFRS- R total score in the MN- 166 (ibudilast) group compared to the placebo group. The Amyotrophic Lateral Sclerosis Functional Rating Scale- Revised (ALSFRS- R) total score measures the functional activity of an ALS subject. There was also a higher rate of responders on the ALSAQ- 5 score in the MN- 166 (ibudilast) group compared to the placebo group. The Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ- 5) score measures the physical mobility, activities of daily living and independence, eating and drinking, communication, and emotional functioning of an ALS subject. In July 2018, we announced data from ad- hoc subgroup analyses in subjects who had either bulbar onset or upper limb onset in the ALS trial at Carolinas Neuromuscular / ALS- MDA Center. In September 2018, we received feedback from the FDA regarding our clinical development plan for MN- 166 (ibudilast) in ALS. In April 2019, we announced that the FDA completed its review of the protocol and determined that we may proceed with a Phase 2b / 3 clinical trial of MN- 166 (ibudilast) in ALS. In June 2019, we announced that a kick- off meeting for the Phase 2b / 3 clinical trial of MN- 166 (ibudilast) in ALS was held our headquarters in La Jolla, California. In December 2019, we announced that additional analyses of the completed clinical trial of MN- 166 (ibudilast) in ALS was presented at the 30th International Symposium on ALS / MND ~~(amyotrophic lateral sclerosis / motor neurone disease)~~ in Perth, Australia. These analyses evaluated the potential background factors of patients' characteristics that could reasonably predict both ALS disease progression and treatment efficacy. The results of these analyses indicate that the efficacy of MN- 166 (ibudilast) is expected to be more robust in patients with a short ALS history. We have incorporated the conclusions from these analyses into the design of our Phase 2b / 3 clinical trial. In December 2021, we announced that a poster with an overview of our ongoing Phase 2b / 3 clinical trial of MN- 166 (ibudilast) in ALS was presented at the 32nd International Symposium on ALS / MND. In December **2024, a study update and interim analysis of phase 2 / 3 clinical data of MN- 166 (ibudilast) in the COMBAT- ALS trial was presented at the 35th international symposium on ALS / MND at Montreal, Canada. Pre- defined interim analysis was conducted to evaluate the correlation between the six month and twelve month data and assessed the twelve month double blind phase trial design. Positive correlations were observed between the six month and twelve month data for CAFS Score (0. 71) modified CAFS score (0. 70) and ALSFRS- R (0. 69). In December** 2015, we announced that the FDA granted Fast Track designation to MN- 166 (ibudilast) for the treatment of patients with ALS. In March 2016, we announced that we received a Notice of Allowance from the ~~United States Patent and Trademark Office (PTO~~ **USPTO** ~~)~~ for a new patent which covers MN- 166 (ibudilast) for the treatment of ALS. In October 2016, we announced that the FDA granted Orphan- Drug designation to MN- 166 (ibudilast) for the treatment of ALS, which will provide seven years of marketing exclusivity if it is approved for ALS. In December 2016, we announced that the European Commission granted Orphan Medicinal Product Designation for MN- 166 (ibudilast) for the treatment of ALS. In January 2019, we received a Notice of Allowance from the ~~U. S. PTO~~ **USPTO** for a new patent which covers the combination of MN- 166 (ibudilast) and riluzole for the treatment of ALS and other neurodegenerative diseases. In February 2016, we entered into an agreement to collaborate with Massachusetts General Hospital (MGH) to study the effects of MN- 166 (ibudilast) on reducing brain microglial activation in ALS subjects measured by a positron emission tomography (PET) biomarker. Results of this clinical trial, which we refer to as the ALS / Biomarker study, were presented at the 30th International Symposium on ALS / MND ~~(amyotrophic lateral sclerosis / motor neurone disease)~~ in Perth, Australia in December 2019. In this small study, there was no detectable effect on PBR28- PET uptake or serum NFl but there was a significant reduction in serum MIF, a marker of neuroinflammation. However, because of the open- label design of this study, there was no placebo group to compare with the MN- 166 (ibudilast) group, so it is not possible to draw any definitive conclusions from this study. Methamphetamine Addiction: Methamphetamine is a central nervous system stimulant drug that is similar in structure to amphetamine. It is a Schedule II drug, meaning that it has high abuse potential and low therapeutic potential. According to the Substance Abuse and Mental Health Services Administration' s (SAMHSA) 2022 National Survey on Drug Use and Health, there are approximately 1. 8 million people aged 12 or older with methamphetamine use disorder in the United States. The Rand Corporation has estimated that the economic burden of methamphetamine use in the United States is approximately $ 23. 4 billion. Currently, there is no pharmaceutical treatment approved for methamphetamine dependence. Based on non- clinical results of the effects of MN- 166 (ibudilast) in an animal model of methamphetamine relapse, investigators at UCLA conducted a Phase 1b clinical trial funded by NIDA to examine the safety and preliminary efficacy of MN- 166 (ibudilast) in non- treatment- seeking, methamphetamine- dependent users in an inpatient trial that was completed in 2012. Subsequently, UCLA investigators received NIDA grant funding for a Phase 2 clinical trial to evaluate MN- 166 (ibudilast) in methamphetamine- dependent users in an outpatient trial setting that commenced in 2013. In March 2018, we announced that this trial did not meet the primary endpoint of methamphetamine abstinence confirmed via urine drug screens during the final two weeks of treatment. In

November 2017, we announced a collaboration with Oregon Health & Science University to initiate a biomarker study to evaluate MN- 166 (ibudilast) in methamphetamine use disorder and this study is ongoing. We were granted Fast Track designation from the FDA for MN- 166 (ibudilast) for the treatment of methamphetamine dependence in 2013. Opioid Withdrawal and Dependency: According to the SAMHSA' s 2022 National Survey on Drug Use and Health, there are approximately 5. 6 million people aged 12 or older with prescription pain reliever use disorder and approximately 0. 9 million people aged 12 or older with heroin use disorder in the United States. Access to prescription opioids has recently become more difficult due to more stringent policies on prescribing opioids. An unintended consequence of this policy is increased use of heroin. Heroin is attractive to prescription opioid addicts because it is less expensive and more accessible than prescription opioids. Heroin poses serious health issues, such as risk of HIV and Hepatitis C infection, overdose, and death. There is an urgent, significant unmet medical need for a safe, effective non- addictive, non- opioid therapy for the treatment of prescription opioid and heroin addiction. Investigators at Columbia University and **New York State Psychiatric Institute (** NYSPI **)** previously completed a NIDA- funded, randomized, double- blind, placebo- controlled in- unit Phase 1b / 2a clinical trial to evaluate the ability of MN- 166 (ibudilast) to reduce opioid withdrawal symptoms in humans. Subsequently, investigators at Columbia University and NYSPI conducted a NIDA- funded Phase 2a clinical trial of MN- 166 (ibudilast) for the treatment of prescription opioid or heroin dependence. In March 2016, we announced that positive findings from the results of this completed study in opioid dependence were presented at the Behavior, Biology and Chemistry: Translational Research in Addiction Meeting. Alcohol Addiction: According to SAMHSA' s 2022 National Survey on Drug Use and Health, there are approximately 29. 5 million people aged 12 or older in the United States with alcohol use disorder. The Centers for Disease Control and Prevention (CDC) has reported that excessive alcohol use costs the United States $ 249 billion per year. Medicines that have been approved by the FDA to treat alcohol dependence include Antabuse ® (disulfiram), Vivitrol (naltrexone), Campral ® (acamprosate) and Revia ® (naltrexone). However, the search for a safe and effective drug remains elusive due to limited success of these FDA- approved compounds (Witkiewitz et al., 2012). In a non- clinical trial (Bell et al., 2013), MN- 166 (ibudilast) was examined in rats and mice and was found to reduce alcohol drinking in alcohol- preferring P rats and high-alcohol drinking (HAD1) rats by 50 %, and in mice made dependent on alcohol at doses which had no effect on non- dependent mice. Investigators at UCLA received funding from the NIAAA to conduct a study to evaluate MN- 166 (ibudilast) with a randomized, double- blind, placebo- controlled within- subject crossover design to determine the safety, tolerability and initial human laboratory efficacy of MN- 166 (ibudilast) in a sample of 24 non- treatment seeking individuals with either alcohol abuse or dependence. Results of the alcohol dependence study were presented at the American College of Neuropsychopharmacology (ACNP)' s 54th Annual Meeting in December 2015. MN- 166 (ibudilast), but not placebo, significantly decreased basal, daily alcohol craving over the course of the study ($p < 0. 05$). MN- 166 (ibudilast) did not affect cue- and stress- induced alcohol craving. However, MN- 166 (ibudilast) increased positive mood during both the cue reactivity and stress procedures. MN- 166 (ibudilast) was safe and well- tolerated during the study. In May 2018, we announced plans to initiate an NIH- funded clinical trial of MN- 166 (ibudilast) in alcohol dependence and withdrawal in collaboration with researchers at UCLA. This study was a randomized, double- blind, placebo- controlled Phase 2 trial to evaluate the effect of 14 days of ibudilast treatment on mood, heavy drinking, and neural reward signals in 52 patients with alcohol use disorder (AUD). Positive results of this Phase 2 clinical trial were presented at the American Psychological Association 2020 Annual Convention which was held online in August 2020. Results from this clinical trial were published in June 2021 in Nature' s Translational Psychiatry which included the following: (1) MN- 166 (ibudilast) did not have a significant effect on negative mood; (2) MN- 166 (ibudilast), relative to placebo, reduced the odds of heavy drinking across time by 45 % ($p = 0. 04$); (3) MN- 166 (ibudilast) attenuated alcohol cue-elicited activation in the ventral striatum (VS) (i. e. reduced the rewarding response to alcohol in the brain) compared to placebo ($p = 0. 01$); (4) alcohol cue- elicited activation in the VS predicted subsequent drinking in the MN- 166 (ibudilast) group ($p = 0. 02$), such that individuals who had attenuated VS activation and took MN- 166 (ibudilast) had the fewest number of drinks per drinking day in the week following the scan; and (5) MN- 166 (ibudilast) reduced alcohol craving compared to placebo on non-drinking days ($p = 0. 02$). These findings extend preclinical and human laboratory studies of the utility of ibudilast to treat AUD and suggest a biobehavioral mechanism through which ibudilast acts, namely, by reducing the rewarding response to alcohol cues in the brain leading to a reduction in heavy drinking. In August 2018, we announced a new NIAAA- funded Phase 2b clinical trial of MN- 166 (ibudilast) in alcohol dependence in collaboration with researchers at UCLA. This clinical trial, which has been completed, evaluated whether MN- 166 (ibudilast) would decrease the percentage of heavy drinking days (defined as $\geq$ 5 drinks for men and $\geq$ 4 drinks for women), as compared to placebo, over the course of the 12- week trial. In February 2022, we announced that MN- 166 (ibudilast) was discussed as one of the promising pharmacological agents for the treatment of AUD in the journal Drugs. The publication, which was written by researchers at UCLA, discussed the beneficial effects of MN- 166 (ibudilast) in treating AUD and noted that these effects are thought to be driven by its anti- inflammatory and pro- neurotrophic properties. In April 2022, we announced that a secondary analysis of a Phase 2 clinical trial of MN- 166 (ibudilast) in AUD was published in the journal Alcoholism: Clinical and Experimental Research. The publication, which was written by researchers at UCLA, discussed the results of the secondary analysis and noted that reductions in alcohol craving may represent a primary mechanism of MN- 166 (ibudilast). In December 2022, we announced that positive results from a secondary analysis of a Phase 2 trial of MN- 166 (ibudilast) in AUD were published in The American Journal of Drug and Alcohol Abuse. These results showed that the high baseline C- reactive protein (CRP) group, i. e. the participants with high inflammation, who received MN-166 (ibudilast) had significantly fewer drinks per drinking day compared to the low baseline CRP group who received MN- 166 (ibudilast) ($p = 0. 007$). In January 2023, we announced that the Phase 2b clinical trial of MN- 166 (ibudilast) for the treatment of alcohol use disorder had completed enrollment. In June 2023, we announced results of the Phase 2b clinical trial of MN- 166 (ibudilast) in alcohol use disorder which were presented at the 46th Annual Research Society on Alcoholism (RSA) Scientific Meeting. This study was a randomized, double- blind, placebo- controlled, Phase 2b clinical trial in 102 treatment- seeking men

and women with moderate or severe alcohol use disorder. MN- 166 (ibudilast) was not superior to placebo for the primary objective of reducing percent heavy drinking days. Also, MN- 166 (ibudilast) was not superior to placebo for the secondary endpoints of 1) the number of drinks consumed per day, 2) the number of drinks consumed per drinking day, 3) the percentage of days abstinent, 4) the percentage of subjects with no heavy drinking days, and 5) the percentage of subjects who are abstinent. This trial showed a placebo effect in which both the placebo and MN- 166 (ibudilast) decreased heavy drinking. Chemotherapy-Induced Peripheral Neuropathy: Peripheral neuropathy is a set of symptoms caused by damage to peripheral nerves, the nerves that are away from the brain and spinal cord. Some of the chemotherapy and other drugs used to treat cancer can damage peripheral nerves which carry sensations to the brain and control the movement of the arms and legs. This damage results in chemotherapy- induced peripheral neuropathy (CIPN) which can be a disabling side effect of cancer treatment. Common symptoms of CIPN include pain, burning, tingling, loss of feeling, coordination and balance problems, muscle weakness, trouble swallowing and passing urine, constipation, and blood pressure changes. Severe CIPN may require chemotherapy dose reduction or cessation. According to a meta- analysis which included more than 4, 000 patients, CIPN prevalence was 68 % when measured in the first month after chemotherapy, 60 % at 3 months, and 30 % at 6 months or more (" Incidence, prevalence, and predictors of chemotherapy- induced peripheral neuropathy: A systematic review and meta- analysis, " Seretny M et al 2014). In March 2018, we announced plans to initiate a clinical trial to evaluate MN- 166 (ibudilast) as a treatment for prevention of CIPN which was funded by the University of Sydney Concord Cancer Centre in Australia. This open- label, sequential cross- over pilot study assessed acute neurotoxicity, CIPN, and drug interactions of MN- 166 (ibudilast) in patients with metastatic gastrointestinal cancer (colorectal cancer and upper gastrointestinal cancers) who were receiving oxaliplatin. In September 2020, we announced that positive clinical findings from this clinical trial were published in Cancer Chemotherapy and Pharmacology. Co- administration of MN- 166 (ibudilast) with oxaliplatin resulted in improvement or stabilization of oxaliplatin- induced neurotoxicity in the majority of participants treated with oxaliplatin. According to the Oxaliplatin- Specific Neurotoxicity Scale (OSNS) assessments, 12 out of 14 participants reported acute neurotoxicity (Grade 1 or 2) in both cycles. Of those, ten out of 12 participants were unchanged and two participants had improved symptoms from Grade 2 to Grade 1 with MN- 166 (ibudilast) co- treatment. Acute neurotoxicity, which predicts chronic CIPN, is expected to worsen in patients with continued chemotherapy. Pharmacokinetic analysis indicated no effect of MN- 166 (ibudilast) on systemic exposure of oxaliplatin. In October 2020, we announced plans to initiate a multi- center, placebo- controlled, randomized Phase 2b trial to evaluate MN- 166 (ibudilast) in CIPN, which is funded by the ~~Australasian Gastro- Intestinal Trials Group (~~AGITG ~~)~~. This clinical trial is evaluating MN- 166 (ibudilast) as a potential treatment to reduce acute neurotoxicity severity and CIPN in patients with metastatic colorectal cancer. Degenerative Cervical Myelopathy: ~~Degenerative cervical myelopathy (~~DCM ~~)~~, also known as cervical spondylotic myelopathy, involves spinal cord dysfunction from compression in the neck. **DCM** ~~Degenerative cervical myelopathy~~ is the most common form of spinal cord impairment in adults and results in disability and reduced quality of life. Patients report neurological symptoms such as pain and numbness in limbs, poor coordination, imbalance, and bladder problems. According to the American Association of Neurological Surgeons, more than 200, 000 cervical procedures are performed each year to relieve compression on the spinal cord or nerve roots. There are no pharmaceuticals approved for the treatment of DCM. In August 2018, we announced plans to initiate a clinical trial of MN- 166 (ibudilast) in DCM in collaboration with the University of Cambridge. The trial, which is funded by a grant from the ~~National Institute for Health Research (~~NIHR ~~)~~ in the ~~United Kingdom (~~UK ~~)~~, is evaluating MN- 166 (ibudilast) as an adjuvant treatment for DCM following spinal surgery to determine whether MN- 166 (ibudilast) is more effective than placebo in improving outcomes after spinal surgery. The two co- primary endpoints are (1) the modified Japanese Orthopaedic Association (mJOA) Score, which evaluates motor dysfunction in upper and lower extremities, loss of sensation, and bladder sphincter dysfunction, at six months after surgery; and (2) Visual Analogue Scale (VAS) measure of neck pain at six months after surgery. In May 2019, we announced our participation at the Kick- off Meeting for this Phase 3 clinical trial in DCM, ~~" REgeneration in CErvical DEgenerative Myelopathy (~~RECEDE Myelopathy ~~) "~~ in collaboration with University of Cambridge researchers. In February 2022, we announced that MN- 166 (ibudilast) was discussed as a potential beneficial pharmacological agent for the treatment of DCM in Global Spine Journal. The publication, which was written by researchers at the University of Cambridge, discussed contemporary therapies that may hold therapeutic value and the attributes of MN- 166 (ibudilast) that support its use in DCM. The publication noted that the combination of anti- inflammatory, neuroprotective, and neuroregenerative properties of MN- 166 (ibudilast) leads to attenuation of glial cell activation and is the basis for the ongoing RECEDE Myelopathy trial. Glioblastoma: According to the American Association of Neurological Surgeons, glioblastoma is an aggressive brain tumor that develops from glial cells (astrocytes and oligodendrocytes), grows rapidly, and commonly spreads into nearby brain tissue. The American Brain Tumor Association reports that glioblastomas represent about 14 % of all primary brain tumors. More than 12, 000 cases of glioblastoma are diagnosed each year in the U. S. According to the Glioblastoma Foundation, average life expectancy for glioblastoma patients who undergo treatment is 12- 15 months and only four months for those who do not receive treatment. In June 2017, we announced positive results from an animal model study that examined the potential clinical efficacy of MN- 166 (ibudilast) for the treatment of glioblastoma which were presented at the 2017 ~~American Society of Clinical Oncology (~~ASCO ~~)~~ Annual Meeting. Results of the glioblastoma mouse model study showed that median survival was higher in the group that received combination treatment with MN- 166 (ibudilast) plus temozolomide compared to the group that received temozolomide alone. In May 2018, we announced that the ~~Investigational New Drug Application (~~IND ~~)~~ for MN- 166 (ibudilast) for treatment of glioblastoma was accepted and opened with the FDA. We were also informed by the FDA that the proposed clinical investigation of MN- 166 (ibudilast) in combination with temozolomide for treatment of glioblastoma may proceed. In October 2018, we announced that the FDA granted orphan- drug designation to MN- 166 (ibudilast) as adjunctive therapy to temozolomide for the treatment of glioblastoma. In January 2019, we announced the initiation of enrollment in a clinical trial of MN- 166 (ibudilast) in combination with temozolomide (TMZ ~~,~~ **or** Temodar ®) for the treatment of glioblastoma at the Dana-

Farber Cancer Institute in Boston. In February 2019, we announced that Scientific Reports published results from the animal model study evaluating MN- 166 (ibudilast) in glioblastoma. The article, " Ibudilast sensitizes glioblastoma to temozolomide by targeting ~~Macrophage Migration Inhibitory Factor (~~MIF ~~)~~, " is the first publication reporting the potential clinical utility of MN- 166 (ibudilast) for glioblastoma. In June 2020, we announced that positive preclinical findings were published in Frontiers in Immunology regarding the prospect of MN- 166 (ibudilast) as an adjunctive treatment for glioblastoma. The publication, entitled " Glioblastoma myeloid- derived suppressor cell subsets express differential macrophage migration inhibitory factor receptor profiles that can be targeted to reduce immune suppression ", was based on our collaboration with the Cleveland Clinic. In August 2021, we announced completion of a safety review of Part 1 of the Phase 2 clinical trial of MN- 166 (ibudilast) in combination with temozolomide, which enrolled 15 subjects with recurrent glioblastoma. There were no concerning safety signals observed in Part 1 and there were no serious adverse events related to MN- 166 (ibudilast). Five out of 15 subjects completed cycle 6 without disease progression, i. e. 33 % of subjects were progression- free at six months. In January 2023, we announced that the Phase 2 clinical trial evaluating MN- 166 (ibudilast) in combination with temozolomide in glioblastoma at the Dana- Farber Cancer Institute had completed enrollment. In February 2023, we announced the presentation of new data regarding a tumor tissue analysis from this clinical trial at the 20th Annual World Congress of SBMT ~~(Society for Brain Mapping and Therapeutics)~~. In November 2023, we announced new data and results of the Phase 2 clinical trial of MN- 166 (ibudilast) in glioblastoma patients at the 28th Annual Meeting of the ~~Society for Neuro- Oncology (~~SNO ~~)~~. The primary endpoints of this Phase 2 clinical trial were safety and tolerability of MN- 166 (ibudilast) and ~~temozolomide (~~TMZ ~~)~~ combination treatment and efficacy of the combination treatment defined as progression- free survival rate at 6 months using the RANO criteria. MN- 166 (ibudilast) and TMZ combination treatment was safe and well- tolerated, and no unexpected adverse effects were reported. The trial enrolled a total of 62 patients, including 36 newly diagnosed glioblastoma patients and 26 recurrent glioblastoma patients. Progression- Free Survival at 6 months (PFS6) was 44 % for newly diagnosed glioblastoma patients and 31 % for recurrent glioblastoma patients. Immunohistochemistry evaluation determined that CD3 expression was a good predictor for tumor progression at five months in recurrent glioblastoma patients treated with MN- 166 (ibudilast) and TMZ as patients with progression had higher CD3 tumor infiltration than patients with no progression ($p < 0.05$). The presentation also included data from preclinical studies which evaluated the combination of MN- 166 (ibudilast) and anti- PD1 or anti- PD- L1 therapy in glioblastoma models. In the first preclinical glioblastoma model study, median survival was 17 days for the vehicle and 28 days for the anti- PD1 inhibitor treatment alone. The addition of MN- 166 (ibudilast) to the anti- PD1 inhibitor treatment significantly extended survival to a median of 66 days ($p < 0.001$) for the combination therapy. In the second preclinical glioblastoma model study, median survival was 18 days for the vehicle and 26 days for the anti- PD- L1 inhibitor treatment alone. The addition of MN- 166 (ibudilast) to the anti- PD- L1 inhibitor treatment significantly extended survival to a median of 34 days ($p < 0.05$) for the combination therapy. **We presented new data and results of a Phase 1b / 2a Clinical Trial of MN- 166 (ibudilast) in glioblastoma at the ASCO Annual meeting 2024 held in Chicago, IL.** In April 2022, we announced that data demonstrating that MN- 166 (ibudilast) prevents metastasis in a ~~uveal melanoma (~~UM ~~)~~animal model was published in the journal Molecular Cancer Research. The publication, which was written by researchers at Columbia University Medical Center, discussed the metastatic UM mouse model study in which quantified bioluminescence signal intensity in the abdominal region was dramatically reduced by MN- 166 (ibudilast) treatment ($p < 0.05$). The publication also noted that histological analysis of the liver tissues of control mice showed the presence of tumor cell clusters which were not present in the liver tissues of mice treated with MN- 166 (ibudilast). Prevention of ARDS in patients with COVID- 19: ARDS is a serious lung condition that causes low blood oxygen. Difficulty breathing is usually the first symptom of ARDS. Infections are the most common risk factors for ARDS and these infections may include influenza, coronavirus, or other viruses. According to the ARDS Foundation, there are an estimated 150, 000 ARDS cases per year in the U. S. and the rate of death is approximately 40 % for ARDS patients. In March 2020, we announced plans to initiate development of MN- 166 (ibudilast) for severe pneumonia and ARDS based on positive results of a preclinical study in an animal model of ARDS (Yang et al., 2020). Results of this preclinical study showed that MN- 166 (ibudilast) treatment reversed histological changes observed in the ARDS mouse model including inflammation, hemorrhage, alveolar congestion, and alveolar wall edema. Importantly, pulmonary edema was significantly reduced by MN- 166 (ibudilast) treatment ($p < 0.001$). In addition, MN- 166 (ibudilast) significantly reduced the levels of inflammatory cytokines including TNF- alpha ($p < 0.001$), IL- 1beta ($p < 0.001$), IL- 6 ($p < 0.001$), and MCP- 1 ($p < 0.001$) in a dose- dependent manner, indicating that ibudilast suppressed the inflammatory response. Results of this study also suggest that MN- 166 (ibudilast) protects against pulmonary injury by attenuating cell apoptosis in lung tissue. In addition to data from the animal model of ARDS, MN- 166 (ibudilast) has been identified as a compound with potential anti- SARS- CoV- 2 activity in an in vitro study which screened 1, 520 compounds for SARS- CoV- 2 replication inhibition (Touret et al., 2020). In April 2020, we announced plans to initiate a clinical trial of MN- 166 (ibudilast) for ARDS caused by COVID- 19. In July 2020, we announced that the IND for MN- 166 (ibudilast) for prevention of ARDS was accepted and opened with the FDA. We were also informed by the FDA that the proposed clinical investigation of MN- 166 (ibudilast) for the prevention of ARDS in patients with COVID- 19 may proceed. In April 2022, we announced that the Phase 2 clinical trial of MN- 166 (ibudilast) in hospitalized COVID- 19 patients at risk for developing ARDS had completed enrollment. In June 2022, we announced positive top- line results from this Phase 2 clinical trial. MN- 166 (ibudilast) demonstrated large improvements compared to placebo for all four clinical endpoints analyzed. The trial achieved statistical significance for one of the co- primary endpoints, the proportion of subjects free of respiratory failure at Day 7, with 71 % of subjects in the MN- 166 (ibudilast) group and 35 % of subjects in the placebo group free of respiratory failure at Day 7 ($p = 0.02$). For the co- primary endpoint of clinical status (i. e., improvement on NIAID scale) at Day 7, 71 % of subjects in the MN- 166 (ibudilast) group and 47 % of subjects in the placebo group had improved clinical status at Day 7 ($p = 0.08$). The trial achieved statistical significance for the proportion of subjects discharged from the hospital with 65 % of subjects in the MN- 166 (ibudilast) group and 29 % of subjects in the placebo group

discharged from the hospital at Day 7 (p = 0. 02). In addition, 0 % of subjects in the MN- 166 (ibudilast) group and 24 % of subjects in the placebo group had worsened clinical status at Day 7 (p = 0. 05). There were two deaths in the placebo group and no deaths in the MN- 166 (ibudilast) group. There were no serious adverse events related to MN- 166 (ibudilast). In July 2022, we announced the initiation of a first- in- human clinical study to evaluate a new parenteral (injectable) formulation of MN- 166 (ibudilast). This formulation will provide an additional option for health care providers to administer MN- 166 (ibudilast) in addition to the oral formulation. In January 2023, we announced that the Phase I clinical trial of MN- 166 (ibudilast) 10 mg ~~intravenous (IV)~~ infusion in healthy volunteers was completed with a favorable safety profile and was well tolerated. Chlorine Gas- Induced Lung Injury: Chlorine gas is a toxic chemical that can be released in industrial accidents and terrorist attacks. Inhalation of chlorine gas causes damage to the respiratory tract and can result in acute lung injury. In March 2021, we announced a partnership with the ~~Biomedical Advanced Research and Development Authority (BARDA)~~, part of the ~~Administration for Strategic Preparedness and Response (ASPR)~~ in the U. S. Department of Health and Human Services, to develop MN- 166 (ibudilast) as a potential ~~medical countermeasure (MCM)~~ against chlorine gas- induced lung damage such as ARDS and ALI. Under the Division of Research, Innovation, and Ventures' (DRIVe) Repurposing Drugs in Response to Chemical Threats (ReDIRECT) program, BARDA agreed to provide federal funding for proof- of- concept studies of MN- 166 (ibudilast) in preclinical models of chlorine gas- induced acute lung injury under Contract No. 75A50121C00022. MN- 166 (ibudilast) was the first compound to receive BARDA' s development support through the DRIVe ReDIRECT program. In September 2023, we announced the results of the nonclinical studies conducted under our contract with BARDA. The primary endpoint of the first nonclinical efficacy study was the pulmonary function measure PaO2 / FiO2, which is the ratio of arterial oxygen partial pressure to fractional inspired oxygen. In the pilot design single- dose treatment regimen, MN- 166 (ibudilast) high dose and the positive control rolipram were more efficacious than MN- 166 (ibudilast) low dose and the negative control until 12 hours after chlorine exposure but this did not yield statistically significant results for overall pulmonary function. In the multi- dose study, each treatment was given every 12 hours with a total of 4 doses after the chlorine gas challenge. Treatment with MN- 166 (ibudilast) high dose resulted in greater improvement (p = 0. 0001) in the mean PaO2 / FiO2 ratio than MN- 166 (ibudilast) low dose, rolipram, and the negative control. The mean PaO2 / FiO2 ratio decreased (worsened) by 57 % from 518. 7 mmHg at baseline (the end of the chlorine gas exposure) to 224. 8 mmHg at hour 48 in the negative control group. The mean PaO2 / FiO2 ratio decreased (worsened) by 36 % from 516. 0 mmHg at baseline to 327. 8 mmHg at hour 48 in the MN- 166 (ibudilast) high dose group. At hour 48, the last time point measured in the study, the mean PaO2 / FiO2 ratio was 46 % higher (better) in the MN- 166 (ibudilast) high dose group than in the negative control group (327. 8 vs. 224. 8 mmHg). Since ARDS is defined as a PaO2 / FiO2 ratio less than 300 mmHg, the mean PaO2 / FiO2 ratio values indicate that the negative control group was still categorized as having mild ARDS at the end of the 48- hour evaluation period but the MN- 166 (ibudilast) high dose group had recovered enough to no longer be defined as having ARDS. MN- 166 (ibudilast) was well tolerated and no safety concerns were observed in the first nonclinical efficacy study. After multiple attempts by our subcontractor to establish the feasibility of the second chlorine- gas induced lung injury model, it was not deemed to be a feasible model to evaluate a drug candidate and there are no evaluable efficacy results. Long COVID: Long COVID includes a wide range of ongoing respiratory, neurologic, and other symptoms that can last for weeks, months, or years following SARS- CoV- 2 infection. According to the ~~U. S. Centers for Disease Control and Prevention (CDC)~~, the prevalence of long COVID is approximately 11 % among adults reporting previous COVID- 19. In August 2022, we announced plans to participate in RECLAIM ~~(Recovering from COVID- 19 Lingering Symptoms Adaptive Integrative Medicine Trial~~ **trial** ~~)~~, a grant- funded, multi- center, randomized, clinical trial to evaluate MN- 166 (ibudilast) and other therapies for the treatment of Long COVID, the lingering symptoms of COVID- 19. We reached an agreement to collaborate with the University Health Network, an academic health sciences center located in Toronto, which has the largest hospital- based research program in Canada. In February 2023, we announced that Health Canada completed its review of the clinical trial application and granted authorization to commence the RECLAIM trial and this study is ongoing ~~. MN- 221 (bedoradrine) is a novel, highly selective beta- 2- adrenergic receptor agonist which has been developed for the treatment of acute exacerbations of asthma. We licensed MN- 221 (bedoradrine) from Kissei Pharmaceutical Co., Ltd. (Kissei) in February 2004. In October 2022, we terminated this license agreement and we have no further financial obligation to Kissei. Current inhaled beta- agonist treatments for asthma exacerbations are limited by bronchoconstriction or insufficient airflow due to inflammation and airway constriction, which reduces the amount of inhaled drug that can get into the lungs. In addition, the amount of inhaled treatments a patient can tolerate is limited due to the potential for cardiovascular side effects (e. g. increased heart rate). MN- 221 (bedoradrine) is designed to treat acute exacerbations of asthma via intravenous (i. v.) infusion, bypassing constricted airways to deliver the drug to the lungs. Preclinical studies showed MN- 221 (bedoradrine) to have a high affinity for the ß2- adrenergic receptor, found primarily in the lungs, and a much lower affinity for the ß1- adrenergic receptor found primarily in cardiac tissue. MN- 221 (bedoradrine)' s improved delivery to the lungs and its cardiac safety profile has potential to help fill an unmet need for patients with acute exacerbations of asthma, helping them to breathe easier and avoid a costly hospital stay. Acute Exacerbation of Asthma: According to the most recent data available from the CDC, there were 939, 000 emergency department visits due to asthma in 2021 and 3, 517 deaths due to asthma in 2021. We completed a Phase 2b randomized, double- blind, placebo- controlled clinical trial which evaluated MN- 221 (bedoradrine) in 175 patients with acute exacerbations of asthma in the emergency department setting. MN- 221 (bedoradrine) did not statistically meet the primary endpoint, improvement in FEV1 (Forced Expiratory Volume in One Second) compared to placebo. However, MN- 221 (bedoradrine) treatment demonstrated statistically significant improvements in endpoints associated with Dyspnea Index scores. MN- 221 (bedoradrine) treatment significantly increased (improved) the change from baseline in Dyspnea Index scale score over Hours 0- 3 compared to placebo (based on AUC [0- 3 hr], p = 0. 0405), significantly increased the change from baseline in Dyspnea Index scale scores at Hour 2 compared to placebo (based on mean score, p = 0. 0042), and significantly increased the percentage of subjects who had improvement in the Dyspnea Index score ≥ 1 point at Hour 2~~

compared to placebo (p = 0. 0323). A post- hoc analysis was performed to evaluate the Treatment Failure rate defined as the number of subjects who were either hospitalized or who returned to the emergency department during the course of the study. In subjects who received corticosteroids greater than 3 hours prior to study drug infusion, the number of treatment failures was significantly greater in the placebo group (74 %) versus the MN- 221 (bedoradrine) group (43 %), p = 0. 0489. No safety / tolerability issues of clinical significance were observed. In October 2012, we met with the FDA to review future development of this product candidate. The FDA identified the risk / benefit profile of MN- 221 (bedoradrine) as a focal point for further development and advised that a clinical outcome, such as a reduction in hospitalizations, would need to be a primary endpoint in a pivotal trial. We have decided that any future MN- 221 (bedoradrine) development will be designed based on the feedback received from the FDA and that any future MN- 221 (bedoradrine) clinical trial development for asthma will be partner- dependent from a funding perspective . MN- 001 (tipelukast) is a novel, orally bioavailable small molecule compound which exerts its effects through several mechanisms to produce its anti- fibrotic and anti- inflammatory activity in preclinical models, including leukotriene (LT) receptor antagonism, inhibition of PDEs (mainly 3 and 4), and inhibition of 5- lipoxygenase (5- LO). The 5- LO / LT pathway has been postulated as a pathogenic factor in fibrosis development and the inhibitory effect of MN- 001 (tipelukast) on 5- LO and the 5- LO / LT pathway is considered to be a novel approach to treat fibrosis. MN- 001 (tipelukast) has been shown to down- regulate expression of genes that promote fibrosis including LOXL2, Collagen Type 1 and TIMP- 1. MN- 001 (tipelukast) has also been shown to down- regulate expression of genes that promote inflammation including CCR2 and MCP- 1. In addition, histopathological data shows that MN- 001 (tipelukast) reduces fibrosis in multiple animal models. We licensed MN- 001 (tipelukast) from Kyorin in 2002. In addition to granting MN- 001 (tipelukast) Fast Track designation for the treatment of NASH with fibrosis, the FDA has also granted MN- 001 (tipelukast) Orphan- Drug designation and Fast Track designation for the treatment of idiopathic pulmonary fibrosis (IPF). Previously, we evaluated MN- 001 (tipelukast) for its potential clinical efficacy in asthma and completed a Phase 2 study in asthma with positive results. MN- 001 (tipelukast) has been administered to more than 600 subjects and is considered generally safe and well- tolerated. Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (: NAFLD): Nonalcoholic fatty liver disease (NAFLD) is a condition in which there is fat in the liver. Some individuals with NAFLD can develop nonalcoholic steatohepatitis (NASH), a condition in which there is fat in the liver along with inflammation and damage to liver cells. NASH is a common liver disease that resembles alcoholic liver disease but occurs in people who drink little or no alcohol. According to the United States National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NASH prevalence in adults in the United States is 1. 5- 6. 5 %, and approximately 24 % of U. S. adults have nonalcoholic fatty liver disease (NAFLD). The underlying cause of NASH is unclear, but it most often occurs in persons who are middle- aged and overweight or obese. Many patients with NASH have elevated serum lipids, diabetes or pre- diabetes. Progression of NASH can lead to liver cirrhosis. Liver transplantation is the only treatment for advanced cirrhosis with liver failure. At this time, there is no pharmaceutical treatment approved for NAFLD or NASH. We completed a preclinical study evaluating the potential clinical efficacy of MN- 001 (tipelukast) for the treatment of NASH. MN- 001 (tipelukast) administered orally once daily (10, 30, and 100 mg / kg for three weeks) was evaluated in the STAM ™ (NASH- HCC) mouse model of NASH, as measured by liver biochemistry and histopathology, NAFLD activity score (NAS), and percent of fibrosis and gene expression. MN- 001 (tipelukast), in a dose- dependent manner, significantly reduced fibrosis area compared with placebo ($p < 0. 01$) as demonstrated by a reduction in liver hydroxyproline content, supporting the anti- fibrotic properties of MN- 001 (tipelukast). MN- 001 (tipelukast) significantly improved NAS ($p < 0. 01$). MN- 001 (tipelukast), in this animal model, improved NASH pathology by inhibiting hepatocyte damage ($p < 0. 01$) and ballooning ($p < 0. 01$). At the same time, MN- 001 (tipelukast) was also shown to reduce certain gene expression levels in the liver, thus implying that MN- 001 (tipelukast) reduces the formation of fibrosis in the NASH model. We completed a second preclinical study that examined the potential clinical efficacy of MN- 001 (tipelukast) for the treatment of advanced NASH. This study used mice in more advanced stages of NASH as compared to the first study of MN- 001 (tipelukast) in a NASH mouse model. MN- 001 (tipelukast) showed anti- NASH and anti- fibrotic effects in the advanced NASH mouse model. NAFLD activity score (NAS) was significantly reduced in the MN- 001 (tipelukast)- treated group compared to the non- treated group ($p < 0. 001$). The reduction was observed consistently in all NAS components including hepatocyte ballooning score ($p < 0. 001$), lobular inflammation score ($p < 0. 01$), and steatosis score ($p < 0. 05$). Percent fibrosis area was also reduced in the MN- 001 (tipelukast) treated group ($p < 0. 01$). In addition, alpha- SMA- positive staining area was significantly reduced in the MN- 001 (tipelukast)- treated group ($p < 0. 001$). Collectively, these results provided compelling evidence that MN- 001 (tipelukast) warrants further evaluation for the treatment of NASH in humans. We have an open IND and the FDA has approved three different Phase 2 clinical trial protocols for MN- 001 (tipelukast) for the treatment of NASH and NAFLD in the United States. In April 2018, we announced that we would terminate early the Phase 2 clinical trial of MN- 001 (tipelukast) in NASH and NAFLD patients with hypertriglyceridemia based on the significant positive results from an interim analysis. This data was presented at the International Liver Congress 2018, the 53rd annual meeting of the European Association for the Study of the Liver (EASL) in Paris, France in April 2018. The FDA has granted Fast Track designation to MN- 001 (tipelukast) for the treatment of patients with NASH with fibrosis. In November 2020, we announced positive results of in- vitro and in- vivo studies that evaluated MN- 001 (tipelukast) for its anti- liver fibrotic effect in human hepatic stellate cells (HSCs) and in an acute liver injury model at the annual meeting of the American Association for the Study of Liver Diseases (AASLD). MN- 001 attenuated TGFβ1 induced HSC activation, TGFβ1 mediated increase in HSC motility and contractility, and fibrogenic signaling in a mouse acute carbon tetrachloride (CCl_4)- induced liver injury model. These data provide additional scientific evidence to support MN- 001' s anti- fibrotic effects in the liver. In November 2021, we announced new findings from a study that investigated the mechanism by which MN- 001 (tipelukast) alters triglyceride metabolism in hepatocytes at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). This study found that MN- 001 (tipelukast) had an inhibitory effect on triglyceride synthesis in HepG2 cells derived from human hepatocellular carcinoma samples. The

expression of CD36, one of the fatty acid transporters involved in the uptake of arachidonic acid into liver cells, was suppressed by adding MN- 001 (tipelukast). This suggests that MN- 001 (tipelukast) reduces triglyceride synthesis by inhibiting arachidonic acid uptake into hepatocytes. CD36 enhances cellular fatty acid uptake in the liver and is known to be involved in the pathogenesis of fatty liver. In April 2022, we announced that the FDA completed its review of a proposed Phase 2 clinical trial to evaluate MN- 001 (tipelukast) for the treatment of patients with NAFLD, type 2 diabetes mellitus, and hypertriglyceridemia and the study may proceed. This multi- center, two- arm, randomized, double- blind, placebo- controlled Phase 2 trial will evaluate MN- 001 (tipelukast) vs. placebo in approximately 40 patients in the U. S. Patients will be randomized 1: 1 to receive either 500 mg / day of MN- 001 (tipelukast) or placebo for 24 weeks. The co- primary endpoints are (1) change from baseline in liver fat content at Week 24, and (2) change from baseline in fasting serum triglycerides at Week 24. In July 2022, we announced the initiation of this Phase 2 clinical trial to evaluate MN- 001 (tipelukast) for the treatment of patients with NAFLD, type 2 diabetes mellitus, and hypertriglyceridemia. In December 2022, we announced the presentation of positive results from a subgroup analysis of the completed Phase 2 clinical trial which evaluated MN- 001 (tipelukast) in participants with NAFLD and hypertriglyceridemia (HTG) at the International Diabetes Federation (IDF) World Diabetes Congress 2022. Compared to subjects without Type 2 diabetes mellitus (T2DM), the T2DM group showed a greater reduction in serum triglyceride levels at Week 8 (50. 8 % reduction for with T2DM versus 17. 8 % reduction for without T2DM, p = 0. 098). Mean HDL increase was significantly greater in subjects with T2DM than subjects without T2DM at Week 8 (15. 8 % versus 1. 0 %, p < 0. 0002). In comparison to subjects without T2DM, the T2DM group showed a greater reduction in serum LDL levels at Week 8 (15. 4 % versus 6. 7 %) . Idiopathic Pulmonary Fibrosis (IPF): Pulmonary fibrosis (PF) is a progressive disease characterized by scarring of the lungs that thickens the lining, causing an irreversible loss of the tissue' s ability to transport oxygen. The causes of PF vary and can be due to anti- cancer drug therapy or exposure to chemicals. Idiopathic pulmonary fibrosis (IPF) is one type of PF without a clear cause. According to the U. S. National Library of Medicine, IPF affects approximately 100, 000 people in the United States, and 30, 000 to 40, 000 new cases are diagnosed annually. The prognosis for IPF is poor and most IPF patients survive only three to five years after diagnosis. We completed a preclinical study evaluating the potential clinical efficacy of MN- 001 (tipelukast) for the treatment of pulmonary fibrosis. MN- 001 (tipelukast), which was administered orally once daily (30, 100 and 300 mg / kg) for two weeks, was evaluated in a mouse model of bleomycin- induced pulmonary fibrosis (PF) as measured by CT evaluation of lung density, degree of pulmonary fibrosis using the Ashcroft score based on histopathological staining, and hydroxyproline content, which is an indicator of fibrosis or storage of collagen in tissue. MN- 001 (tipelukast) significantly decreased the Ashcroft score compared to the Vehicle- treated group (p < 0. 05) after two weeks of treatment and MN- 001 (tipelukast) reduced lung density when compared to the Vehicle- treated group. Moreover, lung hydroxyproline content was significantly reduced compared to the Vehicle- treated group (p < 0. 01). These results show that treatment with MN- 001 (tipelukast) has significant anti- fibrogenic effects in bleomycin- induced pulmonary fibrosis in mice. We have an open IND and the FDA approved a Phase 2 clinical trial protocol for MN- 001 (tipelukast) for the treatment of IPF. A Phase 2 clinical trial of MN- 001 (tipelukast) in IPF was completed at Penn State and we announced results of this trial in August 2021. Although there were no clinically meaningful trends in favor of MN- 001 (tipelukast) for the majority of the clinical outcome measures in this small study of 15 subjects, there were no worsening IPF events (acute IPF exacerbation or hospitalization due to respiratory symptoms) in the MN- 001 (tipelukast) group compared to one worsening IPF event in the placebo group. MN- 001 (tipelukast) demonstrated a substantial reduction in LOXL2, a biomarker for IPF, whereas LOXL2 increased in the placebo group. MN- 001 (tipelukast) was safe and well tolerated. The FDA has granted Orphan- Drug designation to MN- 001 (tipelukast) for treatment of IPF. Orphan- Drug designation will provide seven years of marketing exclusivity for MN- 001 (tipelukast) for the treatment of IPF if it is approved for this indication. The FDA has also granted Fast Track designation to MN- 001 (tipelukast) for the treatment of patients with IPF. MN- 029 (denibulin) is a novel tubulin binding agent (TBA) under development for the treatment of solid tumors. It exerts its activity through reversible inhibition of tubulin polymerization resulting in disruption of the cell cytoskeleton, which causes the cancer cells to deform in shape and ultimately leads to extensive central necrosis of the solid tumor. We licensed MN- 029 (denibulin) from Angiogene Pharmaceuticals, Ltd. (Angiogene) in 2002. Several preclinical pharmacology studies have assessed the mechanism of action and anti- tumor activity of MN- 029 (denibulin) in vivo in rodent models of breast adenocarcinoma, colon carcinoma, lung carcinoma and KHT sarcoma. In these studies, MN- 029 (denibulin) damaged poorly formed tumor blood vessels by weakening tumor blood vessel walls and causing leakage, clotting and eventual vascular shutdown within the tumor, in addition to the direct effect over tumor cells. These studies suggest that MN- 029 (denibulin) acts quickly and is rapidly cleared from the body, which may reduce the potential for some adverse effects commonly associated with chemotherapy. Shutdown of tumor blood flow in tumor models was confirmed through the use of dynamic contrast- enhanced magnetic resonance imaging. In two Phase I clinical studies we conducted, MN- 029 (denibulin) was well- tolerated at doses that reduced tumor blood flow. The first Phase 1 trial determined the safety, tolerability, and maximum tolerated dose (MTD) level of single doses of MN- 029 (denibulin) given every three weeks in 34 subjects with refractory cancer. The MTD was determined to be 180 mg / m2 and appeared to be safe as a single i. v. dose administered every three weeks for as many as 25 cycles. There were no clinically significant changes in routine laboratory assessments, vital signs, or ECG monitoring. The most commonly reported adverse events (AEs) were similar to other chemotherapies- vomiting, nausea, diarrhea, and fatigue. There was a total of nine serious adverse events (SAEs) and study discontinuations due to AEs. In a preliminary evaluation of anti- tumor activity, no patient had a complete response or partial response; however stable disease was seen in 12 patients. MN- 029 (denibulin) had a desired vascular effect in seven of 11 patients that were administered drug at dose levels of ≥ 120 mg / m2. Nine patients continued into extended cycles of treatment. The second Phase 1 study was conducted to determine the safety, tolerability and MTD of single doses of MN- 029 (denibulin) given every seven days for a total of three doses (Days 1, 8 and 15), followed by 13- day recovery (Days 16- 28) in subjects with advanced / metastatic solid tumor cancer. Subjects who tolerated treatment with MN- 029 (denibulin) could

~~receive additional cycles. All 20 subjects reported at least one AE related to the study drug. The most common AEs considered related to the study drug were vomiting, nausea, arthralgia and headache. There were no clinically significant changes in routine laboratory assessments, vital signs, or ECG monitoring. There was one SAE considered unrelated to the study drug. Consistent with the previous Phase 1 trial, MN- 029 (denibulin) up to dose levels of 180 mg / m2 appeared to be safe and well tolerated. One subject had a partial response which lasted for 74 days. Stable disease was observed in seven subjects. The results suggested an effect of MN- 029 (denibulin) on vascular perfusion; however, a larger sample size is warranted. In January 2014, we were granted a new patent from the United States Patent and Trademark Office which covers MN- 029 (denibulin) di-hydrochloride. The patent, which will expire no earlier than July 2032, has claims that cover a compound, pharmaceutical composition, and method of treating certain cell proliferation diseases, including solid tumors, based on denibulin di-hydrochloride. We have filed patent applications based on this U. S. patent in certain foreign countries, and most of them have been granted~~ . Table 1: MN- 166 (ibudilast) Clinical Trials and Programs Indication Clinical Study Institution and Funding Agency (s) Status Long COVID Recovering from COVID- 19 Lingering Symptoms Adaptive Integrative Medicine (RECLAIM) Trial Multicenter University Health Network Ongoing COVID- 19 Primary Progressive and Secondary Progressive Multiple Sclerosis A Randomized, Double- Blind, Placebo- Controlled, Parallel Group Study to Evaluate the Efficacy, Safety, Tolerability, Biomarkers and PK of MN- 166 (Ibudilast) in COVID- 19 Subjects at Risk for Developing ARDS A Randomized, Double- Blind, Placebo- Controlled Study to Evaluate the Safety, Tolerability and Activity of Ibudilast (MN-166) in Subjects with Progressive Multiple Sclerosis MulticenterMediciNova, Inc. Cleveland Clinic / MulticenterNational Institute on Neurological Diseases and StrokeMediciNova, Inc. Completed Completed Amyotrophic Lateral Sclerosis (ALS) A Single- Center, Randomized, Double- Blind, Placebo- Controlled, Six Month Clinical Trial Followed by an Open- Label Extension to Evaluate the Safety, Tolerability, and Clinical Endpoint Responsiveness of Ibudilast (MN- 166) in Subjects with Amyotrophic Lateral Sclerosis (ALS) Carolinas HealthCare System Neurosciences InstituteMediciNova, Inc. Completed ALS / Biomarker A Biomarker Study to Evaluate MN- 166 (ibudilast) in Subjects with Amyotrophic Literal Sclerosis (ALS) Massachusetts General HospitalMediciNova, Inc. Completed Amyotrophic Lateral Sclerosis (ALS) A Phase 2b / 3, Multi-Center, Randomized, Double- Blind, Placebo- Controlled, 12 Month Clinical Trial to Evaluate the Efficacy and Safety of MN-166 (ibudilast) Followed by an Open- Label Extension in Subjects with Amyotrophic Lateral Sclerosis MulticenterMediciNova, Inc. Ongoing Degenerative Cervical Myelopathy A multi- centre, double- blind, randomized, placebo- controlled trial assessing the efficacy of Ibudilast as an adjuvant treatment to decompressive surgery for degenerative cervical myelopathy University of Cambridge / MulticenterNational Institute for Health Research (NIHR) in the U. K. Ongoing Chemotherapy- Induced Peripheral Neuropathy A pilot study evaluating the impact of ibudilast on prevention of chemotherapy- induced acute neurotoxicity and evaluating pharmacokinetics with oxaliplatin in gastro- intestinal cancer patients receiving oxaliplatin University of SydneyConcord Cancer Centre in Australia Completed Chemotherapy- Induced Peripheral Neuropathy Glioblastoma Can Oxaliplatin neurotoxicity be reduced with ibudilast in people with metastatic colorectal cancer – a phase II randomized study Phase 1b / 2a Multi- center, Open- label, Dose Escalation Study to Evaluate the Safety, Tolerability **University of SydneyAustralasian Gastro- Intestinal Trials Group in Australia Dana- Farber Cancer InstituteMediciNova, Inc. Ongoing Completed** and Efficacy of MN- 166 (ibudilast) and Temozolomide Combination Treatment in Patients With Glioblastoma **Substance** ~~University of SydneyAustralasian Gastro- Intestinal Trials Group in Australia Dana- Farber Cancer InstituteMediciNova, Inc. Ongoing CompletedSubstance~~ Dependence / Addiction: Methamphetamine Dependence Randomized Trial of Ibudilast for Methamphetamine Dependence UCLANational Institute on Drug Abuse CompletedMethamphetamine Dependence / Biomarker Effect of Ibudilast on Neuroinflammation in Methamphetamine Users Oregon Health & Science University OngoingOpioid Dependence Effects of Ibudilast (MN- 166), a Glial Activation Inhibitor, on Oxycodone Self- Administration in Opioid Abusers Columbia University / NYSPINational Institute on Drug AbuseMediciNova, Inc. CompletedAlcohol Dependence Development of Ibudilast (MN- 166) asa Novel Treatment for Alcoholism UCLANational Institute on Alcohol Abuseand Alcoholism Completed Alcohol Dependence and Withdrawal Alcohol Dependence Ibudilast (MN- 166) and Withdrawal- Related Dysphoria Ibudilast (MN- 166) for the Treatment of Alcohol Use Disorder UCLANational Institute on Drug Abuse UCLANational Institute on Alcohol Abuseand Alcoholism Completed Completed Sales and Marketing We currently have no marketing and sales capabilities and we expect to rely on strategic partners to commercialize our products. Manufacturing We rely on third parties to manufacture bulk active pharmaceutical ingredients (API) and finished investigational products for research, development, preclinical and clinical trials. We expect to continue to rely on third party manufacturers for the manufacture of the API and finished products for our clinical and any future commercial production requirements. We believe that there are several manufacturing sources available at commercially reasonable terms to meet our clinical requirements and any future commercial production requirements for the API of our products and the finished drug products. For the MN- 166 (ibudilast) development program, we have historically sourced and imported delayed- release ibudilast capsules, marketed in Japan as Pinatos ®, from Taisho Pharmaceutical Co., Ltd. (Taisho). In addition, we use contract manufacturers to manufacture API and finished product for the MN- 166 (ibudilast) development program. Intellectual Property and License Agreements Since our inception in September 2000, we have entered into license agreements with pharmaceutical companies which cover our current product candidates. We have also entered into license agreements with universities which cover additional intellectual property related to our product candidates. In general, we seek to procure patent protection for our anticipated products, or obtain such protection from the relevant patents owned by our licensors. We hold ~~28~~ **40** issued U. S. patents and have filed ~~9~~ **4** additional U. S. patent applications. We also hold ~~122~~ **124** issued foreign patents and ~~28~~ **26** pending foreign patent applications corresponding to these U. S. patents and patent applications. We are not aware of any third party infringement of the patents owned or licensed by us and are not party to any material claims by third parties of infringement by us of such third parties' intellectual property rights. The following is a description of our existing license agreements and intellectual property rights for each of our clinical product candidates. On

October 22, 2004, we entered into an exclusive license agreement with Kyorin for the development and commercialization of MN- 166 (ibudilast). Kyorin is a fully integrated Japanese pharmaceutical company and is listed on the Tokyo Stock Exchange. We obtained an exclusive, worldwide (excluding Japan, China, South Korea and Taiwan), sub- licensable license to the patent rights related to MN- 166 (ibudilast) for the treatment of MS, except for ophthalmic solution formulations. MN- 166 (ibudilast) is not covered by a composition of matter patent. The United States method of use patent for MN- 166 (ibudilast) in MS underlying the license expired on August 10, 2018. Corresponding method of use patents in certain foreign countries also expired on August 10, 2018. Under the terms of the agreement, we granted to Kyorin an exclusive, royalty- free, sub- licensable license to use the preclinical, clinical and regulatory databases to develop ophthalmic products incorporating the MN- 166 (ibudilast) compound anywhere in the world and non- ophthalmic products incorporating the MN- 166 (ibudilast) compound outside of our territory. The license agreement may be terminated by either party following an uncured breach of any material provision in the agreement by the other party. We may terminate the agreement for any reason with 90 days' written notice to Kyorin or, in the event that a third party claims that MN- 166 (ibudilast) infringes upon such third party' s intellectual property rights, with 30 days' written notice. The term of this agreement is determined on a country- by- country basis and extends until the later of the expiration of the obligation to make payments under the agreement or the last date on which the manufacture, use or sale of the product would infringe a valid patent claim held by Kyorin but for the license granted by the agreement or the last date of the applicable market exclusivity period. In the absence of a valid patent claim and generic competition in a particular country, the agreement will expire on the earlier of five years from the date of the first commercial sale of the product by us or the end of the second consecutive calendar quarter in which generic competition exists in such country. Under the license agreement, we have paid Kyorin $ 700, 000 to date, and we are obligated to make payments of up to $ 5. 0 million based on the achievement of certain clinical and regulatory milestones. We are also obligated to pay a royalty on net sales of the licensed products. We own, co- own or hold licenses to ~~16~~ **21** issued U. S. patents and ~~8~~ **4** pending U. S. patent applications as well as ~~48~~ **50** issued foreign patents and ~~23~~ **21** pending foreign patent applications covering MN- 166 (ibudilast) and its analogs. These patents and patent applications are related to our development portfolio and are primarily directed to methods of treating various indications using MN- 166 (ibudilast) and its analogs. We have been granted a U. S. patent which covers the use of MN- 166 (ibudilast) for the treatment of progressive forms of MS. This patent will expire no earlier than November 2029, not including a potential extension under patent term restoration rules, and covers a method of treating PPMS or SPMS by administering MN- 166 (ibudilast). Counterparts of this patent application have been granted in certain foreign jurisdictions. We have been granted a U. S. patent which covers the combination of MN- 166 (ibudilast) and interferon- beta for the treatment of progressive MS, including both PPMS and SPMS, and it expires no earlier than October 2039. We have been granted a U. S. patent which covers the use of MN- 166 (ibudilast) for the treatment of amyotrophic lateral sclerosis (ALS) and it expires no earlier than January 2029. We have been granted a U. S. patent which covers the combination of MN- 166 (ibudilast) and riluzole for the treatment of ALS and other neurodegenerative diseases and it expires no earlier than November 2035. Counterparts of this patent application have been granted in certain foreign jurisdictions. We have been granted two U. S. patents which cover the use of MN- 166 (ibudilast) as part of a combination treatment for glioblastoma and these patents expire no earlier than February 2039. We have been granted a U. S. patent which covers the use of MN- 166 (ibudilast) for the treatment of drug addiction or drug dependence or withdrawal syndrome and it expires no earlier than January 2030. Counterparts of this patent application have been granted in certain foreign jurisdictions. We have been granted a U. S. patent which covers the use of MN- 166 (ibudilast) for the treatment of neuropathic pain and it expires no earlier than December 2025. We have been granted a U. S. patent which covers the use of MN- 166 (ibudilast) for the treatment of an ophthalmic disease / disorder or injury associated with a neurodegenerative disease / disorder or a neuro- ophthalmologic disorder and it expires no earlier than October 2039 ~~. On February 25, 2004, we entered into an exclusive license agreement with Kissei for the development and commercialization of MN- 221 (bedoradrine). In October 2022, we terminated this license agreement and we now have no further financial obligation to Kissei. Following termination of the license agreement, Kissei transferred to us the drug master file for MN- 221 (bedoradrine), all related communications with FDA and all related ownership rights. We have no further obligations to Kissei in connection with developing and commercializing MN- 221 (bedoradrine). We have filed patent applications in the United States and certain foreign countries regarding additional uses and formulations of MN- 221 (bedoradrine). We have been granted a U. S. patent which covers the use of MN- 221 (bedoradrine) for the treatment of acute exacerbations of asthma and it expires no earlier than November 2030. This patent includes claims covering the use of MN- 221 (bedoradrine) in combination with a standard of care treatment regimen and covers different routes of administration, including intravenous, oral and inhalation. We have been granted a U. S. patent that covers the use of MN- 221 (bedoradrine) for the treatment of irritable bowel syndrome and it expires no earlier than April 2031~~ . On March 14, 2002, we entered into an exclusive license agreement with Kyorin for the development and commercialization of MN- 001 (tipelukast). We obtained an exclusive, worldwide (excluding Japan, China, South Korea and Taiwan) sub- licensable license to the patent rights and know- how related to MN- 001 (tipelukast) and its active metabolite, MN- 002, disclosed and included in, or covered by, these patents, in all indications, except for ophthalmic solution formulations. This license included an exclusive, sub- licensable license under two U. S. patents and certain corresponding patents in foreign countries. The United States composition of matter patent for MN- 001 (tipelukast) underlying the license expired on February 23, 2009, and the United States composition of matter patent for MN- 002 underlying the license expired on December 30, 2011. Foreign composition of matter patents for MN- 001 (tipelukast) and MN- 002 have also expired. We own 9 U. S. patents and 65 foreign patents covering certain compositions, uses and manufacturing processes associated with MN- 001 (tipelukast) and MN- 002. Uses covered by these U. S. patents include nonalcoholic steatohepatitis (NASH), advanced NASH with fibrosis, nonalcoholic fatty liver disease (NAFLD), steatosis, hypertriglyceridemia, hypercholesterolemia, hyperlipoproteinemia, fibrosis, ulcerative colitis, interstitial cystitis, and irritable bowel syndrome. Patent applications corresponding to these U. S. patents have been filed in certain foreign countries and some

of the foreign patents have issued. Under the terms of the agreement, we granted to Kyorin an exclusive, royalty- free, sub-licensable license to use the preclinical, clinical and regulatory databases to develop ophthalmic products incorporating MN- 001 (tipelukast) anywhere in the world and non- ophthalmic products incorporating MN- 001 (tipelukast) outside of our territory. The license agreement may be terminated by either party following an uncured breach of any material provision in the agreement by the other party, and we may terminate the agreement for any reason with 90 days' written notice to Kyorin or, in the event that a third party claims that the licensed patent rights or know- how infringe upon such third party' s intellectual property rights, with 30 days' written notice. Under the license agreement, we have paid Kyorin $ 4. 0 million to date, and we are obligated to make payments of up to $ 5. 0 million based on the achievement of clinical and regulatory milestones. We are also obligated to pay a royalty on net sales of the licensed products. ~~On June 19, 2002, we entered into an exclusive license agreement with Angiogene, a privately held, British drug discovery company, for the development and commercialization of the ANG- 600 series of compounds. We obtained an exclusive, worldwide, sub- licensable license to the patent rights and know-how related to the ANG- 600 series of compounds disclosed in and included or covered by these patents for all indications. MN-029 (denibulin) is one of the ANG- 600 series compounds covered by this license. We have been granted a U. S. patent which covers MN- 029 (denibulin) di- hydrochloride and expires no earlier than July 2032. The allowed claims cover a compound, pharmaceutical composition and method of treating certain cell proliferation diseases, including solid tumors, based on denibulin di- hydrochloride. Patent applications corresponding to this U. S. patent were filed in certain foreign countries and patents have been granted in some of those countries. The license agreement may be terminated by either party following an uncured breach of any material provision in the agreement by the other party, and we may terminate the agreement at any time by giving 30 days' advance written notice to Angiogene. The term of this agreement is determined on a country- by- country basis and extends until the earlier of the expiration of the last Angiogene patent (or equivalent) under license which has a valid claim or 15 years from the date of first commercial sale. Under the license agreement, we have paid Angiogene $ 1. 4 million to date and are obligated to make payments of up to $ 16. 5 million based on the achievement of clinical and regulatory milestones. We are also obligated to pay a royalty on net sales of the licensed products.~~ Our proposed commercial activities may conflict with patents which have been or may be granted to competitors, universities and / or others. Third parties could bring legal action against us, our licensors or our sub- licensees claiming patent infringement and could seek damages or enjoin manufacturing and marketing of the affected product or its use or the use of a process for the manufacturing of such products. If any such actions were to be successful, in addition to any potential liability for indemnification, damages and attorneys' fees in certain cases, we could be required to obtain a license, which may not be available on commercially reasonable terms or at all, in order to continue to manufacture, use or market the affected product. We also rely upon unpatented proprietary technology because, in some cases, our interests would be better served by reliance on trade secrets or confidentiality agreements than by patents. However, others may independently develop substantially equivalent proprietary information and techniques or gain access to or disclose such proprietary technology. We may not be able to meaningfully protect our rights in such unpatented proprietary technology. We may also conduct research on other pharmaceutical compounds or technologies, the rights to which may be held by, or be subject to patent rights of, third parties. Accordingly, if products based on such research are commercialized, such commercial activities may infringe patents or other rights, which may require us to obtain a license to such patents or other rights. We are not aware of any third party infringements of patents we hold or have licensed and have not received any material claims by third parties of infringement by us of such parties' intellectual property rights. There can be no assurance that patent applications filed by us or others, in which we have an interest as assignee, licensee or prospective licensee, will result in patents being issued or that, if issued, any of such patents will afford protection against competitors with similar technology or products or could not be circumvented or challenged. For example, we have U. S. patents covering the method of treating progressive MS with MN- 166 (ibudilast), the method of treating ALS with MN- 166 (ibudilast), the method of treating glioblastoma with MN-166 (ibudilast) as part of a combination therapy, the method of treating drug addiction or drug dependence with MN- 166 (ibudilast), and the method of treating neuropathic pain with MN- 166 (ibudilast), but we do not have any composition of matter patent claims for MN- 166 (ibudilast) because that patent has expired. As a result, unrelated third parties may develop products with the same API as MN- 166 (ibudilast) so long as such parties do not infringe our method of use patents, other patents we have exclusive rights to through our licensors or any patents we may obtain for MN- 166 (ibudilast). In addition, if we develop certain products that are not covered by any patents, we will be dependent on obtaining market exclusivity under the new chemical entity exclusivity provisions of the Hatch- Waxman Act for such products in the United States and / or data exclusivity provisions in Europe. If we are unable to obtain strong proprietary protection for our products after obtaining regulatory approval, competitors may be able to market competing generic products by taking advantage of an abbreviated procedure for obtaining regulatory clearance, including the ability to demonstrate bioequivalency to our product (s) without being required to conduct lengthy clinical trials. Certain of our license agreements provide for reduced or foregone royalties in the event of generic competition. Competition The development and commercialization of new drugs is extremely competitive and characterized by extensive research efforts and rapid technological progress. Competition in our industry occurs on a variety of fronts, including developing and bringing new products to market before others, developing new products to provide the same benefits as existing products at lower cost and developing new products to provide benefits superior to those of existing products. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies in the United States and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our product development programs. Many of our competitors have products that have been approved or are in advanced development and may succeed in developing drugs that are more effective, safer, more affordable, or more easily administered than ours or that achieve patent protection or commercialization sooner than our products. Our competitors may also develop alternative therapies that could further limit the market for any products that we are able to obtain approval for, if at all. In many of our target disease areas,

potential competitors are working to develop new compounds with different mechanisms of action and attractive efficacy and safety profiles. Many of our competitors have substantially greater financial, research and development resources (including personnel and technology), clinical trial experience, manufacturing, sales and marketing capabilities and production facilities than we do. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. MN- 166 (ibudilast) for Progressive Multiple Sclerosis (Progressive MS) Our MN- 166 (ibudilast) product candidate is in development for the treatment of progressive MS. Mitoxantrone is approved for the treatment of secondary progressive MS but it cannot be used on a long- term basis because of the potential for cardiac toxicity. There are numerous drugs approved for the treatment of secondary progressive MS with relapses (also known as active secondary progressive MS) including Mayzent (siponimod), Mavenclad (cladribine), Vumerity (diroximel fumarate), Zeposia (ozanimod), Kesimpta (ofatumumab), Bafiertam (monomethyl fumarate), Ponvory (ponesimod), Briumvi (ublituximab- xiiy), Avonex (interferon beta- 1a), Betaseron (interferon beta- 1b), Rebif (interferon beta- 1a), Extavia (interferon beta- 1b), Plegridy (peginterferon beta- 1a), Copaxone (glatiramer acetate), Glatopa (glatiramer acetate), Gilenya (fingolimod), Aubagio (teriflunomide), Tascenso ODT (fingolimod), Tecfidera (dimethyl fumarate), Lemtrada (alemtuzumab), Tysabri (natalizumab) and Tyruko (natalizumab- sztn). Ocrevus (ocrelizumab) is approved for the treatment of primary progressive MS and secondary progressive MS with relapses. There are no drugs specifically approved for the treatment of secondary progressive MS without relapses. Other programs in clinical development for progressive MS include Sanofi' s tolebrutinib, Roche' s fenebrutinib, and AB Science' s masitinib. MN- 166 (ibudilast) for Amyotrophic Lateral Sclerosis (ALS) Our MN- 166 (ibudilast) product candidate is also in development for the treatment of ALS. Generic riluzole, which is also sold under the brand names Rilutek and Tiglutik, Radicava (edaravone), Relyvrio (sodium phenylbutyrate and taurursodiol), and Qalsody (tofersen) are approved for the treatment of ALS. We are aware of additional compounds in clinical development for the treatment of ALS at other companies including BrainStorm Cell Therapeutics, AB Science, Biogen, Ionis Pharmaceuticals, and Clene. MN- 166 (ibudilast) for Substance Dependence and Addiction Our MN- 166 (ibudilast) product candidate is also in development for the treatment of opioid dependence, methamphetamine addiction, and alcohol dependence. Current treatments for opioid withdrawal symptoms include narcotics such as generic methadone and Indivior, Inc.' s Suboxone Film (buprenorphine the opioid antagonist naloxone). Other products approved for opioid dependence include Alkermes' s Vivitrol (naltrexone monthly injection), Orexo' s Zubsolv (buprenorphine and naloxone), and Indivior' s Sublocade (buprenorphine extended- release injection). In May 2023, Braeburn announced FDA approval of BRIXADI (buprenorphine) extended- release injection for subcutaneous use, a new weekly and monthly medication for moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with a transmucosal buprenorphine- containing product. Limited non-narcotic drug candidates for opioid withdrawal symptoms exist. US WorldMeds, LLC' s Lucemyra (lofexidine) is a central alpha- 2 adrenergic agonist approved for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation. There are no pharmaceuticals currently approved for the treatment of methamphetamine addiction. InterveXion Therapeutics is developing a treatment for methamphetamine use disorder. Approved treatments for alcohol dependence include Antabuse (disulfiram), Vivitrol (naltrexone), and generic acamprosate. We are aware of additional treatments in development for the treatment of alcohol use disorder at other companies including Indivior and Adial Pharmaceuticals. MN- 166 (ibudilast) for Chemotherapy- Induced Peripheral Neuropathy Our MN- 166 (ibudilast) product candidate is also in development for the treatment of chemotherapy- induced peripheral neuropathy. There are no pharmaceuticals currently approved for the treatment of chemotherapy- induced peripheral neuropathy. Duloxetine is sometimes used off- label for this indication. We are aware of treatments in development for the treatment of chemotherapy- induced peripheral neuropathy at other companies including AlgoTherapeutix (AlgoTx), Sonnet BioTherapeutics, and WinSanTor. MN- 166 (ibudilast) for Degenerative Cervical Myelopathy Our MN- 166 (ibudilast) product candidate is also in development for the treatment of degenerative cervical myelopathy. There are no pharmaceuticals currently approved for the treatment of degenerative cervical myelopathy. MN- 166 (ibudilast) for Glioblastoma We have initiated clinical development of our MN- 166 (ibudilast) product candidate for the treatment of glioblastoma. Surgery, radiation, and chemotherapy with the drug temozolomide is the current standard of treatment for glioblastoma. GLIADEL ® WAFER (carmustine implant) and AVASTIN ® (bevacizumab) are also approved for the treatment for glioblastoma. We are aware of additional compounds in development for the treatment of glioblastoma at other companies including Kazia Therapeutics, Kintara Therapeutics, Denovo Biopharma, Laminar Pharmaceuticals, and TVAX Biomedical. MN- 166 (ibudilast) for Prevention of ARDS in patients with COVID- 19 Our MN- 166 (ibudilast) product candidate is also in development for the prevention of ARDS in patients with COVID- 19. While we are not aware of any other therapeutics that are in development specifically for this indication, we are aware of other therapeutics approved or in development for the treatment COVID- 19. In October 2020, Gilead Sciences announced FDA approval of its antiviral drug Veklury (remdesivir) for the treatment of patients with COVID- 19 requiring hospitalization. In November 2020, the FDA granted Emergency Use Authorization (EUA) for Eli Lilly' s investigational neutralizing antibody bamlanivimab (LY- CoV555) for the treatment of COVID- 19 patients at high risk for progressing to severe COVID- 19 and / or hospitalization. In November 2020, Eli Lilly and Incyte announced that the FDA issued an EUA for the distribution and emergency use of baricitinib to be used in combination with remdesivir in hospitalized COVID- 19 patients. In November 2020, Regeneron Pharmaceuticals announced that its multi- antibody therapy casirivimab and imdevimab administered together received EUA from the FDA for the treatment of COVID- 19. In February 2021, the FDA issued an EUA for Eli Lilly' s bamlanivimab and etesevimab, administered together, for the treatment of COVID- 19 patients who are at high risk for progression to severe COVID- 19. In May 2021, the FDA issued an EUA for GlaxoSmithKline' s sotrovimab for the treatment of COVID- 19 patients who are at high risk for progression to severe COVID- 19. In June 2021, the FDA issued an EUA for Roche' s Actemra (tocilizumab) for the treatment of hospitalized COVID- 19 patients. In December 2021, Pfizer announced that the FDA granted an EUA for

PAXLOVID (nirmatrelvir tablets and ritonavir tablets) for the treatment of mild to moderate COVID- 19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID- 19. In December 2021, Merck and Ridgeback Biotherapeutics announced that the FDA granted an EUA for molnupiravir, an investigational oral antiviral, to treat mild to moderate COVID- 19 in adults who are at high risk for progression to severe COVID- 19 and for whom alternative COVID- 19 treatment options authorized by the FDA are not accessible or clinically appropriate. In February 2022, the FDA issued an EUA for Eli Lilly' s bebtelovimab for the treatment of mild to moderate COVID- 19 in adults and pediatric patients who are at high risk for progression to severe COVID- 19 and for whom alternative COVID- 19 treatment options are not accessible or clinically appropriate. In November 2022, the FDA issued an EUA for Swedish Orphan Biovitrum' s Kineret (anakinra) for the treatment of hospitalized COVID- 19 adults with pneumonia requiring supplemental oxygen who are at risk for progressing to severe respiratory failure and are likely to have an elevated plasma soluble urokinase plasminogen activator receptor (suPAR). In April 2023, the FDA issued an EUA for InflaRx' s Gohibic (vilobelimab) for the treatment of COVID- 19 in hospitalized adults when initiated within 48 hours of receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (artificial life support). We are aware of additional treatments in development for the treatment of COVID- 19 at other companies including Merck, AstraZeneca, Gilead Sciences, and Rigel Pharmaceuticals. MN- 166 (ibudilast) for Long COVID Our MN- 166 (ibudilast) product candidate is also in development for the treatment of patients with Long COVID, the lingering symptoms of COVID- 19. There are no pharmaceuticals currently approved for the treatment of Long COVID. We are aware of compounds in clinical development for the treatment of Long COVID at other companies including Axcella Therapeutics, AIM ImmunoTech, Tonix Pharmaceuticals, Humanetics, and Aerium Therapeutics. MN- ~~221 (bedoradrine) for Acute Exacerbations of Asthma Our MN- 221 (bedoradrine) product candidate has been developed for the treatment of acute exacerbations of asthma in the emergency room setting. The current standard of care for acute exacerbations of asthma is inhaled albuterol (a beta- 2- adrenergic receptor agonist), inhaled ipratropium (an anticholinergic) and oral or injected corticosteroids. In addition, subcutaneously administered terbutaline (a beta- 2- adrenergic receptor agonist) is sometimes used to treat this condition, particularly in pediatric patients. MN-~~ 001 (tipelukast) for Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (NAFLD) Our MN- 001 (tipelukast) product candidate has been developed for the treatment of NASH and NAFLD. There are currently no pharmaceuticals approved for the treatment of NASH or NAFLD. We are aware of compounds in clinical development for the treatment of NASH or NAFLD at other companies including Galectin Therapeutics, Gilead Sciences, Galmed Pharmaceuticals, Pfizer, Novo Nordisk, Merck, and Madrigal Pharmaceuticals. ~~MN- 001 (tipelukast) for Idiopathic Pulmonary Fibrosis (IPF) Our MN- 001 (tipelukast) product candidate is in development for the treatment of IPF. Products approved in the United States for treatment of IPF include Roche' s (formerly InterMune) Esbriet (pirfenidone) and Boehringer Ingelheim' s OFEV (nintedanib). Companies working on clinical development programs for treatment of IPF include Roche, United Therapeutics, and Bristol- Myers Squibb. MN- 029 (denibulin) for Solid Tumor Cancer Our MN- 029 (denibulin) product candidate has been developed for the treatment of solid tumor cancers. Roche' s Kadcyla, a HER2- targeted antibody and microtubule inhibitor conjugate, is approved for treatment of patients with HER2- positive metastatic breast cancer who previously were treated with trastuzumab and a taxane. Bayer' s Stivarga, a kinase inhibitor approved for metastatic colorectal cancer, was also approved for patients with advanced, unresectable (not subject to surgical removal) or metastatic gastrointestinal stromal tumor. Other drugs approved for solid tumor cancers include Roche' s Avastin and Xeloda, Amgen' s Xgeva, Pfizer' s Sutent, and Novartis' s Afinitor. We are aware of additional compounds in development for the treatment of solid tumor cancers at companies including Eli Lilly, Roche, Novartis, Pfizer, Sanofi, Amgen, Bayer, Merck, AstraZeneca, AbbVie and Bristol- Myers Squibb.~~ Government Regulation Government authorities in the United States and other countries extensively regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution, sampling, marketing and import and export of pharmaceutical products and biologics such as those we are developing. In the United States, the FDA, under the Federal Food, Drug and Cosmetic Act, as amended, and other federal statutes and regulations, subjects pharmaceutical products to extensive and rigorous review. Any failure to comply with applicable requirements, both before and after approval, may subject us, our third party manufacturers, contractors, suppliers and partners to administrative and judicial sanctions, such as a delay in approving or refusal to approve pending applications, fines, warning letters, product recalls, product seizures, total or partial suspension of manufacturing or marketing, injunctions and / or criminal prosecution. United States Regulatory Approval Overview. In the United States, drugs and drug testing are regulated by the FDA under the Federal Food, Drug and Cosmetic Act **(** ~~, or~~ FDCA ~~,~~ **)** as well as state and local government authorities. All our product candidates in development will require regulatory approval by government agencies prior to commercialization. To obtain approval of a new product from the FDA, we must, among other requirements, submit data supporting safety and efficacy, as well as detailed information on the manufacture and composition of the product and proposed labeling. Our product candidates are in the early stages of testing and none has been approved. The steps required before a drug can be approved generally involve the following: • completion of nonclinical laboratory, animal studies, and formulation studies; • submission of an IND application which must become effective before human clinical trials may begin in the United States; • completion of adequate and well- controlled human clinical trials to establish the safety and efficacy of the product candidate for each indication for which approval is sought; • submission to the FDA of a New Drug Application (NDA) accompanied by a substantial user fee; • development of manufacturing processes which conform to FDA-mandated commercial good manufacturing practices (cGMPs) and satisfactory completion of FDA inspections to assess cGMP compliance and clinical investigator compliance with good clinical practices; and • FDA review and approval of an NDA, which process may involve input from advisory committees to the FDA and may include post- approval commitments for further clinical studies and distribution restrictions intended to mitigate drug risks. The testing, collection of data, preparation of necessary applications and approval process requires substantial time, effort and financial resources. Additionally, statutes, rules, regulations and policies may change and new regulations may be issued that could delay approvals of our drugs. The FDA

may not act quickly or favorably in reviewing our applications, and we may encounter significant difficulties and costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our product candidates. Preclinical Tests. Preclinical tests include laboratory evaluation of the product candidate, its chemistry, toxicity, formulation and stability, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the preclinical tests, together with manufacturing information, analytical data and other available information about the product candidate, are submitted to the FDA as part of an IND. Preclinical tests and studies can take several years to complete and, despite completion of those tests and studies, the FDA may not permit clinical testing to begin. The IND Process. An IND must be effective to administer an investigational drug to humans. The IND will automatically become effective 30 days after its receipt by the FDA unless the FDA, before that time, places the IND on clinical hold. At any time thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold if the FDA deems it appropriate. In such case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin or continue. The IND application process may become extremely costly and substantially delay development of our product candidates. Moreover, positive results in preclinical tests or prior human studies do not necessarily predict positive results in subsequent clinical trials. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA and written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events or any findings from tests in laboratory animals that suggest a significant risk for human subjects. Clinical Trials. Human clinical trials are typically conducted in three sequential phases that may overlap: • Phase 1: The drug candidate is initially introduced into a small number of healthy human subjects or patients and tested for safety, dosage tolerance, absorption, distribution, excretion and metabolism. If the investigational product is considered too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in the target population. • Phase 2: The drug candidate is introduced into a limited patient population to assess the efficacy of the drug in specific, targeted indications, assess dosage tolerance and optimal dosage, and to identify possible adverse effects and safety risks. • Phase 3: The drug candidate is introduced into an expanded patient population at geographically dispersed clinical trial sites to further evaluate clinical efficacy and safety. The purpose of the Phase 3 trial is to conduct a risk / benefit analysis of the potential drug and provide an adequate basis for product labeling. It is common to have two adequate and well- controlled Phase 3 trials for the FDA to approve an NDA. Prior to initiation of each clinical trial, an independent Institutional Review Board (IRB) for each medical site proposing to conduct the clinical trials must review and approve the study protocol and study subjects must provide informed consent for participation in the study. We cannot be certain that we will successfully complete Phase 1, 2 or 3 testing of our drug candidates within any specific time period, if at all. Clinical trials must be conducted in accordance with the FDA' s good clinical practices (GCP) requirements. The FDA may order the partial, temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The IRB may also require the clinical trial at that site to be halted, either temporarily or permanently, for failure to comply with the IRB' s requirements, or may impose other conditions. In addition, we may suspend or discontinue a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. During the development of a new drug, we may request to meet with the FDA at times such as prior to submitting an IND, at the End- of- Phase 2 meeting, and before an NDA is submitted, and meetings are not limited to these certain times. The purpose of the End- of- Phase 2 meeting is to discuss the Phase 2 clinical trial results and present plans for a pivotal Phase 3 trial that, in our opinion, will support the approval of the new drug. Additional animal safety studies, formulation studies and pharmacology studies are concurrently conducted with the ongoing clinical trials. Also, in compliance with cGMP requirements, the process for manufacturing commercial quantities of the new drug is finalized, with the expectation that the quality, purity, and potency of the drug will meet standards. A sponsor may also request a Special Protocol Assessment (SPA), the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim. Fast Track Designation: The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life- threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Unique to a Fast Track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. Any product submitted to the FDA for marketing, including a Fast Track program, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an NDA designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug products studied for their safety and effectiveness in treating serious or life- threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well- controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug product receiving accelerated approval perform adequate and well- controlled post- marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre- approval of promotional materials, which could adversely impact the timing of the commercial launch

of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process. United States Patent Term Restoration and Marketing Exclusivity: Depending upon the timing, duration and specifics of the FDA approval of a drug candidate, some U. S. patents covering the product candidates may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product' s approval date. The patent term restoration period is generally one- half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The **USPTO** ~~United States Patent and Trademark Office~~, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent terms for one or more of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of other companies seeking to reference another company' s NDA. The FDCA provides a five- year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA) or a 505 (b) (2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three- year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five- year and three- year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all the preclinical studies and adequate and well- controlled clinical trials necessary to demonstrate safety and effectiveness. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six- month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA- issued " Written Request " for such a trial. Regulation Outside the United States: In addition to regulations in the United States, we and our strategic alliance partners will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, 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. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. To obtain regulatory approval of an investigational drug under European Union regulatory systems, we or our strategic alliance partners must submit a marketing authorization application. The application used to file the NDA in the United States is similar to that required in the European Union, except for, among other things, country- specific document requirements. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we or our strategic alliance partners 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. Human Capital Resources We have assembled an experienced and cohesive management and support team, with core competencies in general management, clinical development, regulatory affairs and corporate development. We have 13 employees as of the date of this report, all of which are full- time. We believe that our relations with our employees are good, and we have no history of work stoppages. Company Information We were originally incorporated in the State of Delaware in September 2000. Our principal executive offices are located at 4275 Executive Square, Suite 300, La Jolla, CA 92037. Our telephone number is 858- 373- 1500. Our website is www. medicinova. com, which includes links to reports we have filed with the Securities and Exchange Commission (SEC). The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report on Form 10- K. Item 1A. Risk Factors We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business, financial condition and results of operations, and you should carefully consider them.

Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Annual Report on Form 10- K and our other public filings with the **Securities and Exchange Commission (** SEC **)** . Other events that we do not currently anticipate or that we currently deem immaterial may also affect our results of operations and financial condition. Risks Related to Our Business and Industry We have incurred significant operating losses since our inception and expect that we will incur continued losses for the foreseeable future. We have incurred significant net losses since our inception in September 2000. For the years ended December 31, **2024 and** 2023 ~~and 2022~~ , we had a net loss of $ **11. 0 million and $** 8. 6 million ~~and $ 14. 1 million~~ , respectively. As of December 31, ~~2023~~ **2024** and December 31, ~~2022~~ **2023** , our accumulated deficit was $ **426. 8 million and $** 415. 7 ~~million and $ 407. 1~~ million, respectively. We expect to incur substantial net losses for the next several years as we continue to develop certain of our existing product candidates, and over the long- term if we expand our research and development programs and acquire or in- license products, technologies or businesses that are complementary to our own. Additionally, the net losses we incur may fluctuate significantly from quarter to quarter such that a period- to- period comparison of our results of operations may not be a good indicator of our future performance. As of December 31, ~~2023~~ **2024** , we had available cash and cash equivalents of $ ~~51~~ **40** . ~~0~~ **4** million and working capital of $ ~~47~~ **38** . ~~9~~ **1** million. There can be no assurances that there will be adequate financing available to us in the future on acceptable terms, or at all. If we are unable to obtain additional financing, we may have to out- license or sell one or more of our programs or cease operations. Our future cash requirements will also depend on many factors, including: • progress in, and the costs of future planned clinical trials and other research and development activities; • the scope, prioritization and number of our product development programs; • our obligations under our license agreements, pursuant to which we may be required to make future milestone payments upon the achievement of various milestones related to clinical, regulatory or commercial events; • our ability to establish and maintain strategic collaborations, including licensing agreements and other arrangements; • the time and costs involved in obtaining regulatory approvals; • the costs of securing manufacturing arrangements for clinical or commercial production of our product candidates; • the costs associated with any expansion of our management, personnel, systems and facilities; • the costs associated with any litigation; • the costs associated with the operations or wind- down of any business we may acquire; • inflation and rapid increases in interest rates; • the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights; and • the costs of establishing or contracting for sales and marketing capabilities and commercialization activities if we obtain regulatory approval to market our product candidates. We expect our research and development expenses to increase moderately in **2025 relative to** 2024 ~~relative to 2023~~ as we continue development of MN- 166 (ibudilast), MN- 001 (tipelukast), and any other future product candidates. We do expect to continue to incur significant operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing drug products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we have taxable income in the future, utilization of the net operating losses (NOL) and tax credit carryforwards will be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, and similar state provisions due to ownership change limitations that have occurred, which will limit the amount of NOL and tax credit carryforwards that can be utilized to offset future taxable income and tax, respectively. We have conducted a study and determined that, through December 31, ~~2022~~ **2023** , no ownership changes have occurred. There is a risk that additional changes in ownership have occurred since the completion of our analysis. If a requisite ownership change occurs, the amount of remaining tax attribute carryforwards available to offset taxable income and reduce income tax expense in future years may be restricted or eliminated. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows. We will need to obtain additional funding to complete the development and any commercialization of our product candidates, if approved. If we fail to obtain this capital necessary to fund our operations, we will be forced to significantly delay, scale back or eliminate some or all of our clinical or regulatory activities or other operations. We have consumed substantial amounts of capital since our inception in September 2000. As of the date of this report, we believe we have sufficient working capital to fund operations at least through the ~~end~~ **next twelve months following the filing** of ~~2025~~ **this Annual Report on Form 10- K** . Our business will continue to require us to incur substantial research and development expenses. We believe that without raising additional capital from accessible sources of financing, we will not otherwise have adequate funding to continue our operations and to complete the development of our existing product candidates or the commercialization of any products we successfully develop. There is no guarantee that adequate funds will be available when needed from debt or equity financings, arrangements with partners, or from other sources, on terms attractive to us, or at all. The inability to obtain sufficient additional funds when needed to fund our operations would require us to significantly delay, scale back, or eliminate some or all of our clinical or regulatory activities and reduce general and administrative expenses. We do not have any products that are approved for commercial sale and therefore currently generate no revenues from sales of any products and may never generate any revenues from product sales or be profitable in the foreseeable future, if ever. To date, we have funded our operations primarily from sales of our securities and, to a lesser extent, debt financing. We do not have any products that are approved for commercial sale and do not anticipate generating any product revenue unless and until one of our product candidates receives the regulatory approvals necessary for commercialization in one or more jurisdictions. We do not expect to receive any revenues from the commercialization of our product candidates for ~~at least~~ the next several years, if at all. We anticipate that, prior to our commercialization of a product candidate, out- licensing upfront and milestone payments will be our primary source of revenue if we can enter into collaborations, strategic alliances or other agreements that would provide us with such revenues. To obtain revenues from sales of our product candidates, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing and marketing drugs with commercial potential. We may never succeed in these

activities, and we may not generate sufficient revenues to continue our business operations or achieve and maintain profitability. We are largely dependent on the success of our MN- 166 (ibudilast) and MN- 001 (tipelukast) product candidates and we cannot be certain that these product candidates will receive regulatory approval or be successfully commercialized. We currently have no products that are approved for commercial sale and we have never had any products approved for commercial sale. We cannot guarantee that we will ever have any drug products approved for sale. The research, testing, manufacturing, labeling, approval, sales, marketing and distribution of drug products are subject to extensive regulation by the **Food and Drug Administration (** FDA **)** and comparable regulatory authorities in other countries. We are not permitted to market any of our product candidates in the United States **or other jurisdictions** until we submit and receive approval of a New Drug Application (NDA) for a product candidate from the FDA or its foreign equivalent from a foreign regulatory authority **, as applicable** . Obtaining FDA approval is a lengthy, expensive and uncertain process. To date we have invested a substantial majority of our business efforts and financial resources to the development and commercialization of our MN- 166 (ibudilast) and MN- 001 (tipelukast) product candidates. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and commercialize MN- 166 (ibudilast) and MN- 001 (tipelukast) and we cannot accurately predict when or if either MN- 166 (ibudilast) or MN- 001 (tipelukast) will receive regulatory approval. Neither of these product candidates have completed the clinical development process, and therefore we have not submitted an NDA or foreign equivalent or received marketing approval for either product candidate. The clinical development program for our product candidates may not lead to commercial products for a number of reasons, including our clinical trials' failure to demonstrate to the FDA' s satisfaction that the product candidate is safe and effective, or our failure to obtain necessary approvals from the FDA or similar foreign regulatory authorities for any reason. We may also fail to obtain the necessary approvals if we have inadequate financial or other resources to advance our product candidates through the clinical trial process or are unable to secure a strategic collaboration or partnership with a third party. Any failure or delay in completing clinical trials or obtaining regulatory approval for our product candidates in a timely manner would have a material and adverse impact on our business and our stock price. Because the results of early clinical trials are not necessarily predictive of future results, our product candidates we advance into clinical trials in any indication may not have favorable results in later clinical trials, if any, or receive regulatory approval. Our product candidates are subject to the risks of failure inherent in drug development. We will be required to demonstrate through well- controlled clinical trials that our product candidates are safe and effective for use in a diverse population for the relevant target indications before we can seek regulatory approvals for their commercial sale. Success in early clinical trials does not mean that later clinical trials will be successful because product candidates in later- stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing, even at statistically significant levels. For example, we may not be able replicate the positive results from our Phase 2 trial of MN- 166 (ibudilast) in alcohol use disorder in clinical trials for other indications in the future. Clinical trial failure may result from a multitude of factors including flaws in trial design, dose selection, placebo effect, patient enrollment criteria, relatively smaller sample size in earlier trials, and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies have suffered significant setbacks in the advancement of clinical trials, even after earlier clinical trials have shown promising results and we cannot be certain that we will not face similar setbacks. Any of our planned clinical trials for our product candidates may not be successful for a variety of reasons, including the clinical trial designs, the failure to enroll a sufficient number of patients, undesirable side effects and other safety concerns and the inability to demonstrate sufficient efficacy. If a product candidate fails to demonstrate sufficient safety or efficacy, we would experience potentially significant delays in, or be required to abandon, development of such product candidate. Significant clinical trial delays could also allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates and impair our ability to commercialize our product candidates and may harm our business and results of operations. Interim and preliminary" top- line" data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available and is subject to audit and verification procedures that could result in material changes in the final data. We have, and from time to time, we may publicly disclose interim, top- line or preliminary data from the clinical trials we conduct, which are based on a preliminary analysis of then- available data. The final results from these clinical trials and any related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. In addition, interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data becomes available. As a result, the top- line or preliminary results that we report may differ from future results of the same trial, or different conclusions or considerations may qualify such results, once additional data has been received and fully evaluated. Top- line or preliminary data also remains subject to audit and verification procedures that may result in the final data being materially different from the top- line or preliminary data we previously published. As a result, top- line and preliminary data should be viewed with caution until final data is available and published. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top- line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, the product candidates we develop

may be harmed, which could harm our business, financial condition, results of operations and prospects. Our attempts to develop MN- 001 (tipelukast) in **Nonalcoholic Steatohepatitis (** NASH ~~,~~**) and Nonalcoholic Fatty Liver Disease (** NAFLD **)** ~~and IPF~~ may detract from our efforts to develop other product candidates and may limit the effectiveness of our product development efforts as a whole. We have decided to pursue development of MN- 001 (tipelukast) in NASH ~~,~~ **and** NAFLD ~~and IPF~~. These activities may divert financial and management resources from our other product development activities and may limit our ability to complete or continue those other programs. In order to commercialize a therapeutic drug successfully, a product candidate must receive regulatory approval after the successful completion of clinical trials, which can be lengthy, complex and costly, have a high risk of failure and can be delayed or terminated at any time. Our product candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. The process of obtaining FDA and other regulatory approvals is lengthy, costly, time- consuming, uncertain and subject to unanticipated delays. To receive regulatory approval for the commercial sale of any of our product candidates, we must conduct, at our own expense, adequate and well- controlled clinical trials in human patients to demonstrate the efficacy and safety of the product candidate. Clinical testing is complex, expensive, takes many years and has an uncertain outcome. To date, we have obtained regulatory authorization to conduct clinical trials for our product development programs. ~~INDs~~ **Investigational New Drug Applications** were approved by the FDA and are active for our product candidates. It may take years to complete the clinical development necessary to commercialize our product candidates, and delays or failure can occur at any stage, which may result in our inability to market and sell any of our product candidates that are ultimately approved by the FDA or foreign regulatory authorities. Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and / or non- clinical testing. Interim results of clinical trials do not necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials even after obtaining promising results in earlier clinical trials. In addition, any delays in completing clinical trials or the rejection of data from a clinical trial by a regulatory authority will result in increased development costs and could have a material adverse effect on the development of the impacted product candidate. In connection with the conduct of clinical trials for each of our product candidates, we face many risks, including the risks that: • the product candidate may not prove to be effective in treating the targeted indication; • clinical trial participants and / or patients may experience serious adverse events or other undesirable drug- related side effects; • the results may not confirm the positive results of earlier trials; • the FDA or other regulatory authorities may not agree with our proposed development plans or accept the results of completed clinical trials; and • our planned clinical trials and the data collected from such clinical trials may be deemed by the FDA or other regulatory authorities not to be sufficient, which would require additional development for the product candidate before it can be evaluated in late stage clinical trials or before the FDA will consider an application for marketing approval. If we do not complete clinical development of our product candidates successfully, we will be unable to obtain regulatory approval to market products and generate revenues from such product candidates. We may also fail to obtain the necessary regulatory approvals if we have inadequate financial or other resources to advance our product candidates through the clinical trial process. In addition, even if we believe that the preclinical and clinical data are sufficient to support regulatory approval for a product candidate, the FDA and foreign regulatory authorities may not ultimately approve such product candidate for commercial sale in any jurisdiction, which would limit our ability to generate revenues and adversely affect our business. In addition, even if our product candidates receive regulatory approval, they remain subject to ongoing FDA regulations, including obligations to conduct additional clinical trials, changes to the product label, new or revised regulatory requirements for manufacturing practices, written advisements to physicians, and / or a product recall or withdrawal. We are subject to stringent regulation of our product candidates, which could delay the development and commercialization of our product candidates. We, our third party manufacturers, service providers, suppliers and partners, if any, and our product candidates are subject to stringent regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. None of our product candidates can be marketed in the United States until it has been approved by the FDA. None of our product candidates has been approved by the FDA to date, and we may never receive FDA approval for any of our product candidates. Obtaining FDA approval for a product takes many years of clinical development and requires substantial resources. Additionally, changes in regulatory requirements and guidance may occur or new information regarding the product candidate or the target indication may emerge, and we may need to perform additional, unanticipated non- clinical or clinical testing of our product candidates or amend clinical trial protocols to reflect these changes. Any additional unanticipated testing would add costs and could delay or result in the denial of regulatory approval for a product candidate. These regulatory requirements may limit the size of the market for the product candidate or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could substantially reduce or negate our ability to generate revenues from the particular product candidate. In addition, both before and after regulatory approval, we, our partners and our product candidates are subject to numerous FDA requirements, including requirements related to testing, manufacturing, quality control, labeling, advertising, promotion, distribution and export. The FDA' s requirements may change and additional government regulations may be promulgated that could affect us, our partners and our product candidates. Given the number of recent high profile adverse safety events with certain drug products, the FDA may require, as a condition of approval, costly risk management programs, which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, preapproval of promotional materials and restrictions on direct- to- consumer advertising. Furthermore, 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. In order to market any of our products outside of the United States, we and our strategic partners and licensees must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and

additional administrative review periods beyond the requirements of the FDA and the time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the United States. Regulatory approval in one country, including FDA approval in the United States, does not ensure regulatory approval in another. In addition, a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. A product candidate may not be approved for all indications that we request, which would limit the uses of our product and adversely impact our potential royalties and product sales, and any approval that we receive may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post- marketing follow- up studies. If we fail to comply with applicable regulatory requirements in the United States or other countries, we may be subject to regulatory and other consequences, including fines and other civil penalties, delays in approving or failure to approve a product, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, interruption of manufacturing or clinical trials, injunctions and criminal prosecution, any of which would harm our business. Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties. Even if U. S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product' s indicated uses or marketing or impose ongoing requirements for potentially costly post- approval studies, including additional research and development and clinical trials. Any of these restrictions or requirements could adversely affect our potential product revenues. For example, the label ultimately approved for any of our other product candidates or any other product candidates that we may in- license or acquire, if any, may include a restriction on the terms of its use, or it may not include one or more of our intended indications. Our product candidates, if approved, will also be subject to ongoing FDA requirements for the labeling, packaging, storage, advertising, promotion, record- keeping and submission of safety and other post- market information on the drug. In addition, approved products, manufacturers and manufacturers' facilities are subject to continual review and periodic inspections. If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates fail to comply with applicable regulatory requirements, such as **commercial good manufacturing practices (** cGMPs **)** , a regulatory agency may: • issue warning letters or untitled letters; • require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for non- compliance; • impose other civil or criminal penalties; • suspend regulatory approval; • suspend any ongoing clinical trials; • refuse to approve pending applications or supplements to approved applications filed by us; • impose restrictions on operations, including costly new manufacturing requirements; or • seize or detain products or require a product recall. **The FDA policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business. Moreover, 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, statutory, regulatory and policy changes, the FDA' s ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s ability to perform routine functions. In addition, government funding of other government agencies 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. The ability of the FDA and other government agencies to properly administer their functions is highly dependent on the levels of government funding and the ability to fill key leadership appointments, among various factors. Delays in filling or replacing key positions could significantly impact the ability of the FDA and other agencies to fulfill their functions, and could greatly impact healthcare and the pharmaceutical industry. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. Further, three decisions from the U. S. Supreme Court 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. 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. For example, these cases may result in increased litigation by companies against the FDA, and impact the FDA' s authority, lead to uncertainties in the industry, and disrupt the FDA' s normal operations, which could impact the timely review of any regulatory filings or applications we submit to the FDA. Further, if a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.** We have received Fast Track and / or Orphan Drug designation for certain of our product candidates and may seek such designation, breakthrough therapy and / or priority review for other product candidates in the future. We may not receive such designations, and even if we do, we may not maintain such designations, and such designations may not lead to faster development, regulatory review or approval, and will not increase the likelihood that the product candidate will receive

marketing approval. We have received Fast Track designation for certain of our product candidates, including MN- 001 (tipelukast) for the potential treatment of ~~IPF,~~ NASH with fibrosis and MN- 166 (ibudilast) for the potential treatment of progressive MS, the potential treatment of **Amyotrophic Lateral Sclerosis (** ALS **)** , and the potential treatment of methamphetamine dependence and we hope to benefit from the FDA' s ~~fast~~ **Fast** ~~track~~ **Track** and priority review programs. Product candidates with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product candidate and the specific indication for which it is being studied. If any of our product candidates receive Fast Track designation but do not continue to meet the criteria for Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. Furthermore, Fast Track designation does not change the standards for approval. The receipt of Fast Track designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if any product candidate qualifies for Fast Track designation, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Fast Track designation alone does not guarantee qualification for the FDA' s priority review procedures. We have also received Orphan Drug designation for several of our product candidates, including for MN- 166 (ibudilast) for the potential treatment of ALS ~~and as adjunctive therapy to temozolomide for the potential treatment of glioblastoma, and to MN- 001 (tipelukast) for the potential treatment of IPF~~ . We may not be able to obtain or maintain Orphan Drug exclusivity in the United States for those product candidates. We may not be the first to obtain marketing approval of any product candidate for which we have obtained Orphan Drug designation for the orphan- designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek FDA marketing approval for an indication broader than the orphan designated indication. Additionally, any product candidate with Orphan Drug designation may lose such designation if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same drug for the same indication if the FDA concludes that the later drug is shown to be safer, more effective or makes a major contribution to patient care. Orphan Drug exclusive marketing rights in the United States also may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, others may obtain Orphan Drug exclusivity for products addressing the same diseases or conditions as products we are developing, thus limiting our ability to compete in the markets addressing such diseases or conditions for a significant period of time. Orphan Drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review. Under the Orphan Drug Act, the FDA may grant Orphan Drug designation to a drug intended to treat a rare disease or condition or for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for a disease or condition will be recovered from sales in the United States for that drug. 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 the FDA may not approve any other applications, including a full NDA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. We may seek priority review **with the FDA (review within a six- month time frame from the time a complete NDA is accepted for filing compared to 10 months under standard review)** for one or more of our current or future product candidates. Under FDA policies, a product candidate is eligible for priority review ~~, or review within a six- month time frame from the time a complete NDA is accepted for filing,~~ if the product candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. The FDA determines whether a drug qualifies for ~~Priority~~ **priority** ~~Review~~ **review** after an NDA for such drug is submitted to the FDA. Therefore, until NDAs are submitted for our product candidates, we cannot be assured that they will be granted ~~Priority~~ **priority** ~~Review~~ **review** . Additionally, even if ~~Priority~~ **priority** ~~Review~~ **review** is granted for one of our product candidates, the FDA does not always meet its six- month **Prescription Drug User Fee Act (** PDUFA **)** goal date for ~~Priority~~ **priority** ~~Review~~ **review** and the review process is often extended by FDA requests for additional information or clarification. We may seek Breakthrough Therapy designation for one or more of our current or future product candidates. Designation as a Breakthrough Therapy is largely within the discretion of the FDA. Accordingly, even if we believe that a product candidate meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non- expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification and revoke the designation. The FDA has broad discretion whether or not to grant Breakthrough Therapy, Fast Track and / or Orphan Drug designation to any product candidate. Accordingly, even if we believe that a product candidate meets the criteria for designation as a Breakthrough Therapy or Orphan Drug designation, the FDA may disagree and instead determine not to make such designation. Even if we receive breakthrough therapy and / or Orphan Drug designation, the receipt of such designation may not result in a faster development or regulatory review or approval process compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate qualifies as a breakthrough therapy or Orphan Drug, the FDA may later decide that it no longer

meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. The failure to obtain a Breakthrough Therapy, Fast Track and / or Orphan Drug designation or admission for any product candidates we may develop or the inability to maintain that designation for the duration of the applicable period could reduce our ability to make sufficient sales of the applicable product candidate to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition. The FDA may withdraw Fast Track designation if it believes that 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. Fast Track or Breakthrough Therapy designation for our product candidates may not actually lead to a faster review process, and a delay in the review process or in the approval of our product candidates will delay revenue from their potential sales and will increase the capital necessary to fund these product candidate development programs. Any product candidates that we advance into clinical trials may cause undesirable side effects or have other properties that could delay or prevent regulatory approval or commercialization or limit its commercial potential. Undesirable side effects caused by any of our product candidates that we advance into clinical trials could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, or cause us to evaluate the future of our development programs. This, in turn, could prevent us from commercializing the affected product candidate and generating revenues from its sale. In addition, if any product candidates we may develop receives marketing approval and we or others later identify undesirable side effects caused by the product, a number of significant negative consequences could result, including: • regulatory authorities may withdraw their approval of the product or place restrictions on the way it is prescribed; • regulatory authorities may require a larger clinical benefit for approval to offset the risk; • regulatory authorities may require the addition of labeling statements that could diminish the usage of the product or otherwise limit the commercial success of the product; • we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product or implement a risk evaluation and mitigation strategy; • we may choose to discontinue sale of the product; • we could be sued and held liable for harm caused to patients; • we may not be able to enter into collaboration agreements on acceptable terms and execute our business model; and • our reputation may suffer. Delays in the commencement or completion of clinical trials, or suspension or termination of our clinical trials, could result in increased costs to us and delay or limit our ability to obtain regulatory approval for our product candidates. If we experience delays in the commencement or completion of our clinical trials, we could incur significantly higher product development costs and our ability to obtain regulatory approvals for our product candidates could be delayed or limited. The commencement and completion of clinical trials requires us to identify and maintain a sufficient number of study sites and enroll a sufficient number of patients at such sites. We do not know whether enrollment in our future clinical trials for our product candidates will be completed on time, or whether our additional planned and ongoing clinical trials for our product candidates will be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a variety of other reasons, including delays in: • regulatory approval to commence or amend a clinical trial; • reaching agreements on acceptable terms with prospective clinical research organizations or **Contract Research Organizations (CROs)**, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • recruiting and enrolling patients to participate in clinical trials; • retaining patients who have initiated a clinical trial but who may be prone to withdraw due to the treatment protocol, lack of efficacy, personal issues or side effects from the therapy or who are lost to further follow- up; • manufacturing sufficient quantities of a product candidate; and • **Institutional Review Board (IRB)** approval or approval from foreign counterparts to conduct or amend a clinical trial at a prospective site. In addition, a clinical trial may be delayed, suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including: • ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results, which may result in the imposition of a clinical hold on the IND for any clinical trial, as well as the inability to resolve any outstanding concerns with the FDA so that a clinical hold already placed on the IND may be lifted and the clinical trial may begin; • inspections of our own clinical trial operations, the operations of our CROs or our clinical trial sites by the FDA or other regulatory authorities, which may result in the imposition of a clinical hold or potentially prevent us from using some of the data generated from our clinical trials to support requests for regulatory approval of our product candidates; • our failure or inability, or the failure or inability of our CROs, clinical trial site staff or other third party service providers involved in the clinical trial, to conduct clinical trials in accordance with regulatory requirements or our clinical protocols; • lower than anticipated enrollment or retention rates of patients in clinical trials; • new information suggesting unacceptable risk to subjects or unforeseen safety issues or any determination that a clinical trial presents unacceptable health risks; • insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials; • lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties; and • the formulation or dosing regimen of a product candidate may result, unintentionally, in patient non- compliance, leading to low patient retention rates, incomplete data to conduct an adequate analysis, and failure to complete the trial. If we experience delays in the completion of our clinical trials for a product candidate, the commercial prospects for such product candidate may be harmed, we may incur increased costs for development of such product candidate and our ability to obtain regulatory approval for such product candidate could be delayed or limited. Many of the factors that cause or lead to delays in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval for a product candidate. In addition, any amendment to a clinical trial protocol may require us to resubmit our clinical trial protocols to IRBs or their foreign counterparts for reexamination, which may delay or otherwise impact the costs, timing or successful completion of a clinical trial. The loss of any rights to develop and market any of our product candidates could significantly harm our business. We license the rights to certain compounds to develop and market our product candidates. We are obligated to develop and commercialize certain

product candidates in accordance with mutually agreed upon terms and conditions. Our ability to satisfy some or all of the terms and conditions of our license agreements is dependent on numerous factors, including some factors that are outside of our control. Any of our license agreements may be terminated if we breach our obligations under the agreement materially and fail to cure any such breach within a specified period of time. If any of our license agreements is terminated, we would have no further rights to develop and commercialize the product candidate that is the subject of the license. The termination of any of our license agreements could materially and adversely affect our business. **Our business could be** ~~The COVID- 19 global pandemic has~~ adversely ~~impacted and may~~ **affected by the effects of health pandemics or epidemics in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations, which could** materially **affect our operations globally, including at our headquarters in San Diego** and **at our clinical trial sites, as well as the business or operations of our manufacturers, CROs or other third parties with whom we conduct business. Our business, operations and clinical development timelines could be** adversely **affected by health pandemics** ~~impact our business and operations. Any other illness or communicable disease~~ , **epidemics** or any other ~~public~~ health crisis **in regions where we have clinical trial sites or other business operations** , **and** could **cause significant disruption in the** ~~also adversely affect our business, results of~~ operations ~~and financial condition~~ **of CROs upon whom we rely** . **Site initiation** ~~In December 2019, an~~ **and** ~~outbreak~~ **patient enrollment could be delayed or suspended due to prioritization** of **hospital resources toward** ~~COVID- 19 began and, in March 2020,~~ the ~~World Health~~ **health** ~~Organization declared COVID- 19~~ **epidemics or patients not having** a ~~pandemic~~ **desire to enroll in clinical trials due to concerns** . ~~The~~ **For example, during the** COVID- 19 pandemic ~~has negatively impacted the global economy, disrupted global supply chains and created significant volatility and disruption of financial markets. In addition, in response to the COVID- 19 pandemic, many state, local and foreign governments put in place quarantines, executive orders, shelter- in- place orders and similar government orders and restrictions in order to control the spread of the disease. Such orders or restrictions resulted in business closures, work stoppages, slowdowns and delays, work- from- home policies, travel restrictions and cancellation of events, among other effects that impacted our business, personnel, personnel at third- party manufacturing facilities and the availability or cost of materials. The COVID- 19 global pandemic has adversely impacted and may materially and adversely impact our business and operations. For example~~ , we saw a decrease in the number of patient visits at some clinical trial sites, which we believe resulted in slower enrollment in our clinical trials than would have occurred without the **COVID- 19** pandemic **. In addition, some patients may not be able to comply with clinical trial protocols and the ability to conduct follow- up visits with treated patients may be limited if patients do not want to participate in follow up visits due to concerns regarding health epidemics or if quarantines impede patient movement or interrupt healthcare services. There may be shortages in the raw materials used in the manufacturing of our product candidates or laboratory supplies for our preclinical studies and clinical trials, in each case, because of ongoing efforts to address the outbreak** . We could be negatively impacted by any other illness or communicable disease, or any other public health crisis that, like **the** COVID- 19 pandemic, results in economic and trade disruptions, including the disruption of global supply chains. The ~~ultimate~~ **response to a health epidemic may redirect resources with respect to regulatory matters in a way that would adversely** impact ~~of the COVID- 19 pandemic is highly uncertain and subject to sudden change, despite expiration of most of the mandates and a waning effect of the pandemic. Any future impacts could have a material, adverse impact on~~ our ~~liquidity~~ **ability to pursue marketing approvals. In addition** , ~~capital resources, operations~~ **we may face impediments to regulatory meetings** and ~~business and those of the~~ **potential approvals due to measures intended to limit in- person interactions. Furthermore,** third parties **, including manufacturers, medical institutions, clinical investigators, CROs and consultants with whom** we ~~rely~~ **conduct business, are similarly adjusting their operations and assessing their capacity in light of a health epidemic. If these third parties continue to experience shutdowns or business disruptions, our ability to conduct our business in the manner and** on ~~, and~~ **the timelines presently planned** could ~~worsen over time~~ **be materially and negatively impacted** . The extent **to which a health** ~~of the impact of the COVID- 19~~ pandemic ~~on our~~ **or epidemic impacts our business, clinical trials, results of operations and** financial condition ~~, liquidity, and future results of operations, including our ability to continue to advance our product development programs in the expected time frame,~~ will depend on future developments, ~~including the duration and spread of the pandemic and related restrictions on travel and transports, all of~~ which are **highly** uncertain and cannot be predicted ~~. While we do~~ **, including, but** not ~~yet know~~ **limited to,** the ~~full~~ **duration of the pandemic or epidemic, its severity, the actions to contain the virus or address its impact, and how quickly and to what** extent ~~of~~ **government orders and mandates are lifted and normal economic and operating activities can resume. Further, while** the potential **economic impact of any health pandemic or epidemic may be difficult to assess or predict, it could result in significant disruptions of global financial markets, which could reduce our ability to access capital, which could in the** future ~~impacts on~~ **negatively affect our liquidity. To the extent a health pandemic or epidemic adversely affects** our business, **clinical trials** ~~any of these occurrences could significantly harm our business~~ , results of operations and financial condition **, it may** ~~. An extended period of global supply chain and economic disruption could~~ also ~~materially~~ **have the** ~~affect~~ **effect** ~~our business, results~~ of **heightening many** ~~operations, access to sources~~ of ~~liquidity~~ **the other risks described in this " Risk Factors " section. The ultimate impact of a health epidemic is highly uncertain** and ~~financial condition~~ **subject to change** . If our competitors develop and market products more rapidly than we do or that are more effective, safer or more affordable than our product candidates, our commercial opportunities may be negatively impacted. The biotechnology and pharmaceutical industries are highly competitive and subject to rapid and intense technological change. We face, and will continue to face, competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, in the United States and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our product development programs. We cannot assure you that developments by others will not render our product candidates obsolete or noncompetitive. Many of our

competitors have products that have been approved or are in advanced development and may succeed in developing drugs that are more effective, safer, more affordable or more easily administered than ours, or that achieve patent protection or commercialization sooner than our products. Our competitors may also develop alternative therapies that could further limit the market for any product candidates that we are able to obtain approval for, if at all. In addition, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical industry at a rapid pace. These developments may render our product candidates obsolete or noncompetitive. In many of our target disease areas, potential competitors are working to develop new compounds with different mechanisms of action and attractive efficacy and safety profiles. Many of our competitors have substantially greater financial, research and development resources, including personnel and technology, clinical trial experience, manufacturing, sales and marketing capabilities and production facilities than we do. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective and less costly than ours and may also be more successful than us in manufacturing and marketing their products. We also expect to face similar competition in our efforts to identify appropriate collaborators or partners to help develop or commercialize our product candidates. We will depend on strategic collaborations with third party partners to develop and commercialize selected product candidates and will not have control over a number of key elements relating to the development and commercialization of these product candidates if we are able to achieve such third party arrangements. A key aspect of our strategy is to seek strategic collaborations with partners, such as large pharmaceutical companies, that are willing to conduct later- stage clinical trials and further develop and commercialize selected product candidates. To date, we have not entered into any such collaborative arrangements, and we may not be able to enter into any collaborations or otherwise monetize these product candidates on acceptable terms, if at all. By entering into a strategic collaboration with a partner, we may rely on the partner for financial resources and for development, regulatory and commercialization expertise. Even if we are successful in entering into a strategic collaboration for one of our product candidates, we will not have control over a number of key elements relating to the development and commercialization of these product candidates. Further, our partner may fail to develop or effectively commercialize the product candidate because such partner: • does not have sufficient resources or decides not to devote the necessary resources due to internal constraints such as limited cash or human resources; • decides to pursue a competitive potential product developed outside of the collaboration; • cannot obtain the necessary regulatory approvals; • determines that the market opportunity is not attractive; or • cannot manufacture the necessary materials in sufficient quantities from multiple sources or at a reasonable cost. We also face competition in our search for partners from other biotechnology and pharmaceutical companies worldwide, many of whom are larger and able to offer more attractive deals in terms of financial commitments, contribution of human resources, or development, manufacturing, regulatory or commercial expertise and support. If we are not successful in attracting partners and entering into collaborations on acceptable terms for these product candidates or otherwise monetizing these product candidates, we may not be able to complete development of or obtain regulatory approval for such product candidates. In such event, our ability to generate revenues from such products and achieve or sustain profitability would be significantly hindered. We rely on third parties to conduct our clinical trials, and we may incur additional development costs, experience delays in the commencement and completion of clinical trials, and be unable to obtain regulatory approval for or commercialize our product candidates on our anticipated timeline if these third parties do not successfully carry out their contractual duties or meet expected deadlines, which may have an adverse effect on our business and prospects. We do not have the ability to independently conduct our clinical trials. We currently rely extensively on third parties, such as CROs, medical institutions, clinical investigators, contract laboratories and other service providers to perform important functions related to the conduct of our clinical trials, the collection and analysis of data and the preparation of regulatory submissions. Although we design and / or manage our current clinical trials to ensure that each clinical trial is conducted in accordance with its investigational plan and protocol, we do not have the ability to conduct all aspects of our clinical trials directly for our product candidates. We expect to continue to rely upon third parties to conduct additional clinical trials of potential future product candidates. These third parties are not our employees, and except for remedies available to us under our agreements with such third party, we have limited ability to control the amount or timing of resources that any such third party will devote to our clinical trials. Some of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements with a third party, it would delay our development activities. The FDA requires us and our third parties to comply with regulations and standards, commonly referred to as good clinical practices **(** ~~, or~~ GCPs ~~,~~ **)** for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. Our reliance on these third parties does not relieve us of these responsibilities and requirements. The CROs, medical institutions, clinical investigators, contract laboratories and other service providers that we employ in the conduct of our clinical trials are not our employees, and we cannot control the amount or timing of resources that they devote to our product development programs. If any of these third parties fails to devote sufficient care, time and resources to our product development programs, if its performance is substandard, or if any third party is inspected by the FDA and found not to be in compliance with GCPs, it will delay the completion of the clinical trial in which they are involved and the progress of the affected development program. The CROs and other third ~~-~~party service providers with which we contract for execution of our clinical trials play a significant role in the conduct of the clinical trials and the subsequent collection and analysis of data. Any failure of the CROs and other third ~~-~~party service providers to meet their obligations could adversely affect clinical development of our product candidates. Moreover, these third parties may have relationships with other commercial entities, some of which may have competitive products under development or currently marketed, and our

competitive position could be harmed if they assist our competitors. In addition, the operations of our CROs and other third- party service providers may be constrained or disrupted by **widespread health** ~~the COVID- 19 pandemic~~ **pandemics or epidemics** . If any of these third parties does not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for our product candidates. In addition, while we believe that there are numerous alternative sources to provide these services, we might not be able to enter into replacement arrangements without delays or additional expenditures if we were to seek such alternative sources. Switching or adding additional CROs, investigators and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays can occur, which could materially impact our ability to meet our desired clinical development timelines. ~~The COVID- 19 pandemic and government~~ **Government** measures taken in response **to global health pandemics or epidemics** have also had a significant impact on many CROs. Although we plan to carefully manage our relationships with our CROs, investigators and other third parties, we may nonetheless encounter challenges or delays in the future, which could have a material and adverse impact on our business, financial condition and prospects. We rely, and intend to rely, on third party manufacturers to produce our product candidates, which may result in delays in our clinical trials and the commercialization of products, as well as increased costs. We have no manufacturing facilities, and we do not intend to develop facilities for the manufacture of our product candidates for clinical trials or commercial purposes in the foreseeable future. We rely, and expect to continue to rely, on third party manufacturers to produce, in collaboration with us, sufficient quantities of our product candidates for clinical trials, and we plan to contract with third party manufacturers to produce sufficient quantities of any product candidates that may be approved by the FDA or other regulatory authorities for commercial sale. While we believe that there are competitive sources available to manufacture our product candidates, we may not be able to enter into arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty. Reliance on third party manufacturers limits our ability to control certain aspects of the manufacturing process and therefore exposes us to a variety of significant risks, including risks related to our ability to commercialize any products approved by regulatory authorities or conduct clinical trials, reliance on such third parties for regulatory compliance and quality assurance, and the refusal or inability of a third party manufacturer to supply our requirements on a long- term basis. In addition, manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel and compliance with federal, state and foreign regulations. In addition, the **global health** ~~COVID- 19 pandemic~~ **pandemics or epidemics** may impact our third party manufacturers from producing sufficient quantities of any product candidate. Also, our manufacturers may not perform as agreed. If our manufacturers were to encounter any of these difficulties, our ability to timely produce our product candidates for clinical trials and commercial sale may be interrupted, which could result in delayed clinical trials or delayed regulatory approval and lost or delayed revenues. We may not be able to establish or maintain any commercial manufacturing and supply arrangements on commercially reasonable terms that we require for purposes of commercializing a product. Any failure by us to secure or maintain any such required commercial supply agreements could result in interruption of supply and lost or delayed revenues, which would adversely affect our business. Any problems or delays we experience in preparing for commercial- scale manufacturing of a product candidate may result in a delay in FDA or other regulatory approval of the product candidate or may impair our ability to manufacture commercial quantities, which would adversely affect our business. For example, our manufacturers will need to produce specific batches of a product candidate to demonstrate acceptable stability under various conditions and for commercially viable lengths of time. We and our third party manufacturers will need to demonstrate to the FDA and other regulatory authorities this acceptable stability data for the product candidate, as well as validate methods and manufacturing processes, in order to receive regulatory approval to commercialize such product candidate. Our manufacturers are obligated to operate in accordance with FDA- mandated ~~current good manufacturing practices, or~~ cGMPs and, in some cases, International Convention on Harmonization **(** ~~, or~~ ICH **)** , standards. A failure of any of our third party manufacturers to establish and follow cGMPs and / or ICH standards and to document their adherence to such practices may lead to significant delays in our ability to timely conduct and complete clinical trials, obtain regulatory approval of product candidates or launch of our products into the market. In addition, changing third party manufacturers is difficult. For example, a change in third party manufacturer for a particular product candidate requires re- validation of the manufacturing processes and procedures in accordance with cGMPs, which may be costly and time- consuming and, in some cases, our manufacturers may not provide us with adequate assistance to transfer the manufacturing processes and procedures for our product candidates to new manufacturers or may possess intellectual property rights covering parts of these processes or procedures for which we may need to obtain a license. Failure by our third party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of regulatory approvals, seizures or recalls of products, operating restrictions and criminal prosecutions. We, or our third- party manufacturers, may not be able to manufacture our product candidates in sufficient quality or commercial quantities, which would delay or prevent us from commercializing our product candidates. To date, our product candidates have been manufactured in small quantities for preclinical studies and clinical trials. If any of our product candidates is approved by the FDA or comparable regulatory authorities in other countries for commercial sale, we or our third- party manufacturers will need to manufacture such product candidate in larger quantities. We or our third- party manufacturers may not be able to increase successfully the manufacturing capacity for any of our product candidates in a timely or economic manner, or at all. Significant scale- up of manufacturing may require additional validation studies, which the FDA must review and approve. If we or our third- party manufacturers are unable to increase successfully the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply. Our product

candidates require precise, high - quality manufacturing. Our failure to achieve and maintain these high manufacturing standards in collaboration with our third party manufacturers, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could harm our business, financial condition and results of operations. Materials necessary to manufacture our product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our product candidates. We rely on the third party manufacturers of our product candidates to purchase from third party suppliers the materials necessary to produce the **active pharmaceutical ingredients (** API **)** and product candidates for our clinical trials, and we will rely on such manufacturers to purchase such materials to produce the API and finished product for any commercial distribution of our products if we obtain marketing approval. Suppliers may not sell these materials to our manufacturers at the time they need them in order to meet our required delivery schedule or on commercially reasonable terms, if at all. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Moreover, we currently do not have any agreements for the production of these materials. If our manufacturers are unable to obtain these materials for our clinical trials, testing of the affected product candidate would be delayed, which may significantly impact our ability to develop the product candidate. If we or our manufacturers are unable to purchase these materials after regulatory approval has been obtained for one of our products, the commercial launch of such product would be delayed or there would be a shortage in supply of such product, which would harm our ability to generate revenues from such product and achieve or sustain profitability. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates progress through preclinical to late - stage clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates and generate revenue. Our product candidates, if approved for sale, may not gain acceptance among physicians, patients and the medical community, thereby limiting our potential to generate revenues. If any of our product candidates is approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product by physicians, healthcare professionals and third party payers and our profitability and growth will depend on a number of factors, including: • demonstration of efficacy and safety; • changes in the standard of care for the targeted indication; • relative convenience and ease of administration; • the prevalence and severity of any adverse side effects; • availability, cost and potential advantages of alternative treatments, including less expensive generic drugs; • pricing and cost effectiveness, which may be subject to regulatory control; • effectiveness of our or any of our partners' sales and marketing strategies; • publicity concerning our products or competing products; • the product labeling or product insert required by the FDA or regulatory authority in other countries; and • the availability of adequate third party insurance coverage or reimbursement. If any product candidate that we develop does not provide a treatment regimen that is as beneficial as, or is perceived as being as beneficial as, the current standard of care or otherwise does not provide patient benefit, that product candidate, if approved for commercial sale by the FDA or other regulatory authorities, likely will not achieve market acceptance. Our ability to effectively promote and sell any approved products will also depend on pricing and cost-effectiveness, including our ability to produce a product at a competitive price and our ability to obtain sufficient third party coverage or reimbursement. If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, patients and third party payers, our ability to generate revenues from that product would be substantially reduced. In addition, our efforts to educate the medical community and third party payers on the benefits of our product candidates may require significant resources and may never be successful. If our products are not accepted by the market or if users of our products are unable to obtain adequate coverage of and reimbursement for our products from government and other third party payers, our revenues and profitability will suffer. Our ability to commercialize our product candidates, if approved, successfully will depend in significant part on pricing and cost effectiveness, including our ability to produce a product at a competitive price and our ability to obtain appropriate coverage of and reimbursement for our products and related treatments from governmental authorities, private health insurers and other organizations, such as health maintenance organizations **(** ~~, or~~ HMOs **)** . Third party payers are increasingly challenging the prices charged for medical products and services. We cannot provide any assurances that third party payers will consider our products cost- effective or provide coverage of and reimbursement for our products, in whole or in part. Uncertainty exists as to the coverage and reimbursement status of newly approved medical products and services and newly approved indications for existing products. Third party payers may conclude that our products are less safe, less clinically effective or less cost- effective than existing products, and third party payers may not approve our products for coverage and reimbursement. If we are unable to obtain adequate coverage of and reimbursement for our products from third party payers, physicians may limit how much or under what circumstances they will prescribe or administer them. Such reduction or limitation in the use of our products could cause our sales to suffer. Even if third party payers make reimbursement available, payment levels may not be sufficient to make the sale of our products profitable. Market acceptance and sales of our current or future product candidates will depend in large part on global reimbursement policies and may be affected by future health care reform measures, both in the United States and other key international markets. For example, continuing health care reform in the United States will control or significantly influence the purchase of medical services and products, and may result in inadequate coverage of and reimbursement for our products. Many third party payers are pursuing various ways to reduce pharmaceutical costs, including the use of formularies. The market for our products depends on access to such formularies, which are lists of medications for which third party payers provide reimbursement. These formularies are increasingly restricted,

and pharmaceutical companies face significant competition in their efforts to place their products on formularies. This increased competition has led to a downward pricing pressure in the industry. The cost containment measures that third party payers, including government payers, are instituting could have a material adverse effect on our ability to operate profitably. We are dependent on our management team, particularly our President and Chief Executive Officer, and our experienced scientific staff, and if we are unable to retain, motivate and attract key personnel, our product development programs may be delayed and we may be unable to develop successfully or commercialize our product candidates. We are dependent upon the continued services of our executive officers and other key personnel, particularly Yuichi Iwaki, M. D., Ph. D., our founder and our President ~~and~~ **,** Chief Executive Officer **and Chairman of our board of directors** , who has been instrumental in our ability to in- license product candidates from Japanese pharmaceutical companies and secure financing from Japanese institutions. The relationships that certain of our key managers have cultivated with pharmaceutical companies from whom we license product candidates and to whom we expect to out- license product candidates make us particularly dependent upon their continued services with us, whether through employment, service on our board of directors or a consulting agreement. We are also substantially dependent on the continued services of clinical development personnel because of the highly technical nature of our product development programs. We are not presently aware of any plans of our executive officers or key personnel to retire or leave employment. Following termination of employment, these individuals may engage in other businesses that may compete with us. If we acquire or license new product candidates, our success may depend on our ability to attract, retain and motivate highly qualified management and scientific personnel to manage the development of these new product candidates. In particular, our product development programs depend on our ability to attract and retain highly experienced clinical development personnel. However, we face competition for experienced professional personnel from numerous companies and academic and other research institutions. Competition for qualified personnel is particularly intense in the San Diego, California area, where our corporate headquarters is located. In addition, we have scientific and clinical advisors who assist us in our product development and clinical strategies. These third parties are not our employees and may have commitments to, or contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with our product candidates. Although we have employment agreements with key members of management, each of our employees, subject to applicable notice requirements, may terminate his or her employment at any time. We do not carry " key person " insurance covering members of senior management. If we lose any of our key management personnel, we may not be able to find suitable replacements, which would adversely affect our business. If we are unable to establish sales, marketing and distribution capabilities, whether independently or with third parties, we will be unable to commercialize our product candidates successfully. To date, we have not sold, marketed or distributed any pharmaceutical products. If we are successful in obtaining regulatory approvals for any of our product candidates or acquiring other approved products, we will need to establish sales, marketing and distribution capabilities on our own or with partners in order to commercialize an approved product. The acquisition or development of an effective sales and marketing infrastructure will require a significant amount of our financial resources and time and could negatively impact our commercialization efforts, including delay of a product launch. We may be unable to establish and manage a sufficient or effective sales force in a timely or cost- effective manner, if at all, and any sales force we do establish may not be capable of generating demand for our products, therefore hindering our ability to generate revenues and achieve or sustain profitability. In addition, if we are unable to develop internal sales capabilities, we will need to contract with third parties or establish a partnership to market and sell the product. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate any product revenues, may generate increased expenses and may never become profitable. In addition, although we intend to establish strategic collaborations to market any products approved for sale by regulatory authorities outside of the United States, we may be required to market our product candidates outside of the United States directly if we are unable to establish such collaborations. In that event, we may need to build a corresponding international sales and marketing capability with technical expertise and with supporting distribution capabilities. Health care reform measures could adversely affect our business. The business and financial condition of pharmaceutical and biotechnology companies are affected by the efforts of governmental and third party payers to contain or reduce the costs of health care. In the United States and in foreign jurisdictions, there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the health care system. For example, in some countries, pricing of prescription drugs is subject to government control, and we expect to continue to see proposals to implement similar controls in the United States to continue. Another example of proposed reform that could affect our business is drug reimportation into the United States. Moreover, the pendency or approval of such proposals could result in a decrease in our stock price or our ability to raise capital or to obtain strategic partnerships or licenses. More recently, the Patient Protection and Affordable Care Act imposed numerous reforms that may impact the costs, legal requirements and potential success of our operations. Any clinical trial programs, marketing, or research collaborations in the European Economic Area **(EEA)** will subject us to the General Data Protection Regulation, including as implemented in the UK (~~"~~ GDPR ~~"~~). The GDPR applies to companies established in the EEA, as well as to companies that are not established in the EEA and which, inter alia, collect and use personal data in relation to (i) offering goods or services to, or (ii) monitoring the behavior of, individuals located in the EEA. If we conduct clinical trial programs in the EEA (whether the trials are conducted directly by us or through a clinical vendor or collaborator), or enter into research collaborations involving the monitoring of individuals in the EEA, or market our products to individuals in the EEA, we will be subject to the GDPR. The GDPR puts in place stringent operational requirements for processors and controllers of personal data, including, for example, high standards for obtaining consent from individuals to process their personal data (or reliance on another appropriate legal basis), the provision of robust and detailed disclosures to individuals about how personal data is collected and processed (in a concise, intelligible and easily accessible form), a comprehensive individual data rights regime (including access, erasure, objection, restriction, rectification and portability), maintaining a record of data processing, data export restrictions governing transfers of

data from the EEA, short timelines for certain data breach notifications to be given to data protection regulators or supervisory authorities (and in certain cases, affected individuals), and limitations on retention of personal data. The GDPR also puts in place increased requirements pertaining to health data and other special categories of personal data, and includes within scope, pseudonymized (i. e., key- coded) data. Further, the GDPR provides that EEA member states may establish their own laws and regulations limiting the processing of genetic, biometric, or health data, which could limit our ability to collect, use, and share such data and / or could cause our costs to increase. In addition, there are certain obligations if we contract third ~~-~~party processors in connection with the processing of personal data. If our or our collaborators' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data, or fines of up to 20 million Euros or up to 4 % of our total worldwide annual revenue of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, including class- action type litigation, negative publicity, reputational harm and a potential loss of business and goodwill. Additionally, following the United Kingdom' s withdrawal from the European Union, we will have to comply with the GDPR and the GDPR as implemented in the United Kingdom, each regime having the ability to fine up to the greater of € 20 million / £ 17. 5 million, respectively, or 4 % of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains subject to change, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk. We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities. Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release, and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds, and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood- borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions. As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third ~~-~~party manufacturers or our development efforts may be interrupted or delayed. We are subject to certain **United States** ~~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. **United States** ~~U. S.~~ and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations, which we collectively refer to as Trade Laws, prohibit, among other things, 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. Exports of our products are further subject to export controls and sanctions laws and regulations imposed by the **United States** ~~U. S.~~ government and administered by the **United States** ~~U. S.~~ Departments of State, Commerce, and Treasury. **United States** ~~U. S.~~ export control laws may require a license or other authorization to export products to certain destinations and end users. In addition, **United States** ~~U. S.~~ economic sanctions laws include restrictions or prohibitions on engaging in any transactions or dealings, including receiving investment or financing from, or engaging in the sale or supply of products and services to, **United States** ~~U. S.~~ sanctioned countries, governments, persons and entities. 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- **United States** ~~U. S.~~ activities to increase over time. We expect to rely on third parties for research, preclinical studies, and clinical trials and / or to obtain necessary permits, licenses, patent registrations, and other marketing approvals. 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. Any changes in Trade Laws could result in a decreased ability to export or sell our solutions to, existing or potential customers with international operations. Future changes in Trade Laws and enforcement could also result in increased compliance requirements and related costs which could materially adversely affect our business, results of operations, financial condition and / or cash flows. We may be sued for product liability, which could result in substantial liabilities that exceed our available resources and damage our reputation. The development and commercialization of drug products entails significant product liability risks. Product liability claims may arise from use of any of our product candidates in clinical trials and the commercial sale of any approved products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in: • withdrawal of clinical trial participants; • termination of clinical trial sites or entire clinical trial programs; • decreased demand for our product candidates; • impairment of our business reputation; • costs of related litigation; • substantial monetary awards to patients or other claimants; • loss of revenues; and • the inability to commercialize our product candidates. We currently have insurance that covers our clinical trials. We believe our current insurance coverage is reasonably adequate at this time; however, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for all expenses or losses we may suffer. In addition, we will need to increase and expand this coverage as we commence additional clinical trials, as well as larger scale clinical trials, and in the event that any of our product candidates is approved for commercial sale. This insurance may be prohibitively expensive or may not fully cover our potential liabilities. In addition, our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the regulatory approval or

commercialization of products that we or one of our collaborators develop. Successful product liability claims could have a material adverse effect on our business and results of operations. Liability from such claims could exceed our total assets if we do not prevail in any lawsuit brought by a third party alleging that an injury was caused by one of our product candidates. We expect that our results of operations will fluctuate, which may make it difficult to predict our future performance from period to period. Our quarterly operating results have fluctuated in the past and are likely to continue to do so in the future. Some of the factors that could cause our operating results to fluctuate from period to period include: • the status of development of our product candidates and, in particular, the advancement or termination of activities related to our product development programs and the timing of any milestone payments payable under our licensing agreements; • the execution of other collaboration, licensing and similar arrangements and the timing of payments we may make or receive under these arrangements; • variations in the level of expenses related to our product development programs; • the unpredictable effects of collaborations during these periods; • the timing of our satisfaction of applicable regulatory requirements, if at all; • the rate of expansion of our clinical development and other internal research and development efforts; • the costs of any litigation; • the effect of competing technologies and products and market developments; and • general and industry- specific economic conditions. We believe that quarterly or yearly comparisons of our financial results are not necessarily meaningful and should not be relied upon as indications of our future performance. 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 new compliance initiatives. As a public company, we are required to comply with the Sarbanes- Oxley Act of 2002 **(Sarbanes- Oxley Act)** , as well as rules and regulations implemented by the SEC, the Nasdaq Stock Market (Nasdaq) and Japanese securities laws, and incur significant legal, accounting and other expenses as a result. These rules impose various requirements on public companies, including requiring the 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 may make it more difficult and expensive for us to renew our director and officer liability insurance and may result in imposition of reduced policy limits and coverage. The Sarbanes- Oxley Act requires that we (i) maintain effective internal controls for financial reporting and disclosure controls and procedures and (ii) perform an evaluation of our internal control over financial reporting to allow management to report on the effectiveness of those controls, as required by Section 404 **of the Sarbanes- Oxley Act (Section 404)** . Our listing obligations under the Standard Market of the Tokyo Stock Exchange **(,** ~~, or~~ TSE ~~,~~ **)** also require that we comply either with Section 404 ~~of the Sarbanes- Oxley Act~~ or equivalent regulations in Japan and we elected to comply with Section 404. Additionally, we are subject to attestation by our independent registered public accounting firm regarding our internal controls over financial reporting as of December 31, ~~2023~~ **2024** under Japanese securities laws. Our efforts to comply with Section 404 and related regulations have required, and continue to require, the commitment of significant financial and managerial resources. We cannot be certain that a material weakness will not be identified when we test the effectiveness of our controls in the future. If a material weakness is identified, we could be subject to sanctions or investigations by Nasdaq, the SEC, the TSE 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. Additionally, **there are significant corporate governance and executive compensation related provisions** in ~~July 2010,~~ the Dodd- Frank Wall Street Reform and Consumer Protection ~~Act, or the Dodd- Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd- Frank~~ Act that require the SEC to adopt additional rules and regulations in these areas. To maintain high standards of corporate governance and public disclosure, we intend to invest all reasonably necessary resources to comply with such compliance programs and rules and all other evolving standards. These investments may result in increased general and administrative costs and a diversion of our management' s time and attention from strategic revenue generating and cost management activities. We, or our third ~~-~~-party CROs or other contractors or consultants, may be subject to information technology systems failures, network disruptions, breaches in data security and computer crime and cyber- attacks, which could result in a material disruption of our product candidates' development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business. We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third ~~-~~-party contractors who have access to our confidential information. Information technology system failures, network disruptions, breaches of data security and sophisticated and targeted computer crime and cyber- attacks could disrupt our operations by impeding our drug development programs, including delays in our regulatory efforts, the manufacture or shipment of products, the processing of transactions or reporting of financial results, or by causing an unintentional disclosure of confidential information. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. In the ordinary course of our business, we collect and store sensitive data in our data centers and on our networks, including IP, proprietary business information, and personal information of our business partners and employees. Despite our efforts to protect sensitive, confidential or personal data or information, our facilities and systems and those of our third ~~-~~-party service providers may be vulnerable to security breaches, theft, misplaced or lost data, programming and / or human errors that could potentially lead to the compromising of sensitive, confidential or personal data or information, improper use of our systems, software solutions or networks, unauthorized access, use, disclosure, modification or destruction of information,

defective products, production downtimes and operational disruptions, which in turn could adversely affect our reputation, competitiveness and results of operations. While management has taken steps to address these concerns by conducting employee training, implementing certain data and system redundancy, hardening and fail- over along with other network security, comprehensive monitoring of our networks and systems, maintenance of backup and protective systems and other internal control measures, there can be no assurance that the measures we have implemented to date would be sufficient in the event of a system failure, loss of data or security breach. As a result, in the event of such a failure, loss of data or security breach, our financial condition and operating results could be adversely affected. Macroeconomic pressures, **including those** resulting from **ongoing geopolitical matters** ~~health epidemics, including the COVID- 19 pandemic~~ , unfavorable market conditions, **health epidemics, and** regulatory and policy changes ~~, and ongoing geopolitical matters~~ , may have an adverse impact on our business, financial results, stock price and results of operations as well as the business of our current and potential customers. **Our results** ~~While the severity~~ of **operations could be adversely affected by unfavorable global and geopolitical** ~~the COVID- 19 pandemic has lessened significantly, the pandemic has had a significant negative impact on the macroeconomic~~ ----- **economic** ~~environment~~ **conditions** , such as decreases in per capital income and level of disposable income, inflation, rising interest rates, and supply chain issues. Ongoing geopolitical matters have also contributed to difficult macroeconomic conditions and exacerbated supply chain issues, resulting in significant economic uncertainty as well as volatility in the financial markets and new regulatory and policy initiatives particularly in the United States. Such conditions may adversely impact our business, financial results, and prospects and our target customers' businesses. In addition, such macroeconomic conditions could impact our ability to access the public markets as and when appropriate or necessary to carry out our operations or our strategic goals. We cannot predict the ongoing extent, duration or severity of these conditions, nor the extent to which we may be impacted. To the extent macroeconomic conditions worsen, our business, operations and results of operation could be negatively impacted. Additionally, to the extent that there **are health** ~~is a resurgence in the COVID- 19 pandemic~~ **pandemics** , **epidemics** or **any** other health **crisis** ~~epidemics or outbreaks~~ , our operations could be disrupted and our business adversely impacted. Such disruptions or impacts may be similar to those we faced during the COVID- 19 pandemic, such as mandated business closures in impacted areas, limitations with employee resources due to stay at home orders or sickness of employees or their families, reduction of our business operations and the business operations of our targeted utility and critical infrastructure customers, all of which may have an adverse impact on our business, financial results, stock price and results of operations. We may be adversely affected by the effects of inflation. Inflation has the potential to adversely affect our business, results of operations, financial position and liquidity by increasing our overall cost structure, particularly if we are unable to achieve commensurate increases in the prices we charge our customers. The existence of inflation in the economy has the potential to result in higher interest rates and capital costs, supply shortages, increased costs of labor and other similar effects. As a result of inflation, we may experience increases in the costs of labor, materials, and other inputs, such as engineering consultants. Although we may take measures to mitigate the impact of this inflation, if these measures are not effective our business, results of operations, financial position and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these beneficial actions impact our results of operations and when the cost of inflation is incurred. A variety of risks associated with operating our business and marketing our products internationally could materially adversely affect our business. A significant amount of our business activity is outside of the United States. We face risks associated with our international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. We are subject to numerous risks associated with international business activities, including, but not limited to: • compliance with differing or unexpected regulatory requirements for our products; • difficulties in staffing and managing foreign operations; • in certain circumstances, including with respect to the commercialization of our product candidates in Europe, increased dependence on the commercialization efforts of our distributors or strategic partners; • foreign government taxes, regulations and permit requirements; • United States and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements; • economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries; • fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues, and other obligations related to doing business in another country; • compliance with tax, employment, immigration and labor laws, regulations and restrictions for employees living or traveling abroad; • workforce uncertainty in countries where labor unrest is more common than in the United States; • changes in diplomatic and trade relationships; and • challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States **.** These and other risks associated with our international operations may materially adversely affect our business, financial condition and results of operations. Our ability to compete may decline if we do not adequately protect our proprietary rights. There is the risk that our patents (both those owned by us and those in- licensed) may not provide a competitive advantage, including the risk that our patents expire before we obtain regulatory and marketing approval for one or more of our product candidates, particularly our in- licensed patents. Also, our competitors may develop products similar to ours using methods and technologies that are beyond the scope of our intellectual property rights. Composition of matter patents on APIs may provide protection for pharmaceutical products without regard to formulation, method of use, or other type of limitation. We do not have compound patent protection for the API in our MN- 166 (ibudilast) ~~,~~ **and** MN- 001 (tipelukast ~~), and MN- 221 (bedoradrine~~) product candidates, although we do have patent protection for a particular crystalline polymorph of MN- 001 (tipelukast) and we have composition of matter protection on an analog of MN- 166 (ibudilast). As a result, competitors that obtain the requisite regulatory approval will be able to offer products with the same API as found in our MN- 166 (ibudilast) ~~,~~ **and** MN- 001 (tipelukast ~~), and MN- 221 (bedoradrine~~) product candidates so long as such competitors do not infringe any methods of use, methods of manufacture, formulation or, in the case of MN- 001 (tipelukast), specific polymorph patents that we hold or have exclusive rights to through our licensors. For example, we currently rely on method of use patents

for MN- 166 (ibudilast) ~~, and~~ MN- 001 (tipelukast) ~~, and MN- 221 (bedoradrine) although we have a compound patent for MN- 029~~ . It is our policy to consult with our licensors in the maintenance of granted patents we have licensed and in their pursuit of patent applications that we have licensed, but each of our licensors generally remains primarily responsible for or in control of the maintenance of the granted patents. We have limited control, if any, over the amount or timing of resources that each licensor devotes on our behalf. As a result of this lack of control, we cannot be sure that our licensed patents will be maintained and that any additional patents will ever mature from our licensed applications. Issued U. S. patents require the payment of maintenance fees to continue to be in force. We typically rely on our licensors to do this and their failure to do so could result in the forfeiture of patents not timely maintained. Many foreign patent offices also require the payment of periodic annuities to keep patents and patent applications in good standing. As we generally do not maintain control over the payment of annuities, we cannot be certain that our licensors will timely pay such annuities and that the granted patents will not become abandoned. For example, certain annuities were not paid in a timely manner with respect to foreign patents licensed under MN- 002 (the active metabolite of MN- 001 (tipelukast) and, as a result, our patent rights may be impaired in those territories. In addition, our licensors may have selected a limited amount of foreign patent protection, and therefore applications have not been filed in, and foreign patents may not have been perfected in, all commercially significant countries. The patent protection of our product candidates and technology involves complex legal and factual questions. Most of our license agreements give us a right, but not an obligation, to enforce our patent rights. To the extent it is necessary or advantageous for any of our licensors' cooperation in the enforcement of our patent rights, we cannot control the amount or timing of resources our licensors devote on our behalf or the priority they place on enforcing our patent rights. We may not be able to protect our intellectual property rights against third party infringement, which may be difficult to detect, especially for infringement of patent claims for methods of manufacturing. Additionally, challenges may be made to the ownership of our intellectual property rights, our ability to enforce them or our underlying licenses, which in some cases have been made under foreign laws and may provide different protections than that of U. S. law. We cannot be certain that any of the patents or patent applications owned by us or our licensors related to our product candidates and technology will provide adequate protection from competing products. Our success will depend, in part, on whether we or our licensors can: • obtain and maintain patents to protect our product candidates; • obtain and maintain any required or desirable licenses to use certain technologies of third parties, which may be protected by patents; • protect our trade secrets and know- how; • operate without infringing the intellectual property and proprietary rights of others; • enforce the issued patents under which we hold rights; and • develop additional proprietary technologies that are patentable. The degree of future protection for our proprietary rights is uncertain. For example: • we or our licensor might not have been the first to make the inventions covered by each of our pending patent applications or issued patents; • we or our licensor might not have been the first to file patent applications for these inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies; • it is possible that none of our pending patent applications will result in issued patents; • any patents under which we hold rights may not provide us with a basis for maintaining market exclusivity for commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties as invalid, not infringed or unenforceable under **United States** ~~U. S.~~ or foreign laws; or • any of the issued patents under which we hold rights may not be valid or enforceable or may be circumvented successfully in light of the continuing evolution of domestic and foreign patent laws. Changes in patent law in the **United States** ~~U. S.~~ and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. As in the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time- consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the **United States** ~~U. S.~~ could increase the uncertainties and costs. Recent patent reform legislation in the U. S. and other countries, including the Leahy- Smith America Invents Act (Leahy- Smith Act), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy- Smith Act includes a number of significant changes to **United States** ~~U. S.~~ patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost- effective avenues for competitors to challenge the validity of patents. These include allowing third ~~-~~ party submission of prior art to the U. S. Patent and Trademark Office (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. After March 2013, under the Leahy- Smith Act, the **United States** ~~U. S.~~ transitioned to a first inventor to file system in which, assuming that the other statutory requirements 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. However, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. The **United States** ~~U. S.~~ Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Depending on future actions by the **United States** ~~U. S.~~ Congress, the **United States** ~~U. S.~~ courts, the USPTO and the relevant law- making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. The **United States** ~~U. S.~~ federal government retains certain rights in inventions produced with its financial assistance under the Bayh- Dole Act **of 1980 (Bayh- Dole Act)** . The federal government retains a nonexclusive, nontransferable, irrevocable, paid- up license for its own benefit. The Bayh- Dole Act also provides federal agencies with " march- in rights ". March- in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a nonexclusive, partially exclusive, or exclusive license to a responsible applicant or applicants. If the

patent owner refuses to do so, the government may grant the license itself. If, in the future, we co- own or license in technology that is critical to our business that is developed in whole or in part with federal funds subject to the Bayh- Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected. Additionally, the new unitary patent system that came into effect in Europe in June 2023 has increased the complexity and uncertainty of European patent laws and would significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC- based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long- term effects of any potential changes. Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete. Because we operate in the highly technical field of research and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary trade secrets and unpatented know- how. However, trade secrets are difficult to protect, and we cannot be certain that others will not develop the same or similar technologies on their own. We have taken steps, including entering into confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors, to protect our trade secrets and unpatented know- how. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party' s relationship with us. We also typically obtain agreements from these parties which provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Further, we have limited control, if any, over the protection of trade secrets developed by our licensors. Enforcing a claim that a party illegally obtained and is using our trade secrets or know- how is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets or know- how. The failure to obtain or maintain trade secret protection could adversely affect our competitive position. A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business. There is significant litigation in our industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, their methods of use, manufacturing or other technologies or activities infringe the intellectual property rights of such third parties. There are many patents relating to chemical compounds and methods of use. If our compounds or their methods of use or manufacture are found to infringe any such patents, we may have to pay significant damages or seek licenses under such patents. We have not conducted comprehensive searches for unexpired patents issued to third parties relating to our product candidates. Consequently, no assurance can be given that unexpired, third party patents containing claims covering our product candidates, their methods of use or manufacture do not exist. Moreover, because some patent applications in the United States may be maintained in secrecy until the patents are issued, and because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, we cannot be certain that others have not filed patent applications that will mature into issued patents that relate to our current or future product candidates and which could have a material effect in developing and commercializing one or more of our product candidates. The owner of a patent that is arguably infringed can bring a civil action seeking to enjoin an accused infringer from importing, making, marketing, distributing, using or selling an infringing product. We may need to resort to litigation to enforce our intellectual property rights or to seek a declaratory judgment concerning the scope, validity or enforceability of third party proprietary rights. Similarly, we may be subject to claims that we have inappropriately used or disclosed trade secrets or other proprietary information of third parties. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to: • payment of actual damages, royalties, lost profits, potential enhanced damages and attorneys' fees, if any infringement for which we are found liable is deemed willful, or a case against us is determined by a judge to be exceptional; • injunctive or other equitable relief that may effectively block our ability to further develop, commercialize and sell our products; • having to enter into license arrangements that may not be available on reasonable or commercially acceptable terms; or • significant cost and expense, as well as distraction of our management from our business. As a result, we could lose our ability to develop and commercialize current or future product candidates. We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. From time to time, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. Risks Related to the Securities Markets and Investment in Our Common Stock The stock price of our common stock may be volatile or decline regardless of our operating performance, and you may not be able to resell our shares at a profit or at all. Despite the listing of our common stock on the Nasdaq Global Market and the **TSE** ~~Standard Market of the Tokyo Stock Exchange~~ in Japan, trading volume in our securities has been light and

an active trading market may not develop for our common stock. In ~~2023~~ **2024**, our average trading volume was approximately ~~44~~ **49**, ~~278~~ **188** shares per day on **Nasdaq** ~~the NASDAQ Global Market~~ and approximately ~~100~~ **163**, ~~325~~ **556** shares per day on the **TSE** ~~Standard Market~~. The market prices for securities of biopharmaceutical and biotechnology companies, and early- stage drug discovery and development companies like us in particular, have historically been highly volatile and may continue to be highly volatile in the future. For example, since the date of our initial public offering in Japan on February 8, 2005 through December 31, ~~2023~~ **2024**, our common stock has traded as high as approximately $ 42. 00 and as low as approximately $ 1. ~~30~~ **13**. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock, many of which are beyond our control: • the development status of our product candidates, including clinical trial results and determinations by regulatory authorities with respect to our product candidates; • the initiation, termination, or reduction in the scope of any collaboration arrangements or any disputes or developments regarding such collaborations; • FDA or foreign regulatory actions, including failure to receive regulatory approval for any of our product candidates; • announcements of technological innovations, new commercial products or other material events by us or our competitors; • disputes or other developments concerning our intellectual property rights; • market conditions in the pharmaceutical and biotechnology sectors; • actual and anticipated fluctuations in our quarterly or annual operating results; • price and volume fluctuations in the overall stock markets; • changes in, or failure to meet, securities analysts' or investors' expectations of our financial performance; • additions or departures of key personnel; • the economy as a whole and market conditions in our industry ~~, including conditions resulting from COVID- 19~~; • discussions of our business, management, products, financial performance, prospects or stock price by the financial and scientific press and online investor communities; • litigation or public concern about the safety of our potential products; • public concern as to, and legislative action with respect to, the pricing and availability of prescription drugs or the safety of drugs and drug delivery techniques; or • regulatory developments in the United States and in foreign countries. Broad market and industry factors, as well as economic and political factors, also may materially adversely affect the market price of our common stock. Our common stock may be delisted ~~on~~ **from** the Nasdaq Global Market or the Standard Market of the Tokyo Stock Exchange. In addition to the risks identified immediately above, the market price of our common stock, and your ability to sell your shares at a profit, or at all, may be affected by the delisting of our shares for failure to meet applicable listing standards. For example, price per share minimums are maintained by the Nasdaq Global Market, and our share price has, in the past, fallen below the required minimum. Failure to meet these or other listing requirements for either of the stock exchanges on which our common stock is listed could adversely affect the market price for our common stock and your ability to sell your shares at a profit, or at all. The sale of additional common stock, including under our existing shelf registration statement and at market issuance sales agreement may cause substantial dilution to our existing stockholders and / or the price of our common stock to decline. Sales of a substantial number of shares of our common stock could cause our stock price to decline. Sales of a substantial number of shares of our common stock could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of February ~~12~~ **17**, ~~2024~~ **2025**, we had 49, 046, 246 shares of common stock outstanding. Shares held by directors, executive officers and other affiliates will be subject to volume limitations under Rule 144 under the Securities Act and various vesting agreements. Further, we have registered and intend to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of our outstanding warrant or options, or the perception that such sales may occur, could adversely affect the market price of our common stock. We also expect that significant additional capital may be needed in the future to continue our planned operations. On August 26, 2022, we filed a shelf registration statement (Shelf Registration Statement) on Form S- 3 with the SEC (that was declared effective by the SEC on September 6, 2022), which permits us to offer up to $ 200. 0 million of our common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination, including units from time to time. Our Shelf Registration Statement is intended to provide us with flexibility to raise capital in the future for general corporate purposes. As part of this Shelf Registration Statement, we also entered into an amendment to an at market issuance sales agreement (as amended, the ATM Agreement) with B. Riley Securities, Inc. (formerly B. Riley FBR, Inc.) (B. Riley Securities) pursuant to which we may offer and sell common stock through B. Riley Securities from time to time up to an aggregate offering price of $ 75. 0 million, of which $ 10. 3 million of our common stock was sold under a previous shelf registration statement on Form S- 3, which expired on August 22, 2022 (Prior Shelf Registration Statement). In connection with the ATM Agreement and as part of the Shelf Registration Statement, we filed a prospectus supplement to register up to $ 64. 7 million of our common stock, which represents the remaining shares that we previously registered for sale under the sales agreement and the Prior Shelf Registration Agreement. From time to time, we may sell additional shares of our common stock under the Shelf Registration Statement or the ATM Agreement. Depending upon market liquidity at the time, sales of shares of our common stock under the Shelf Registration Statement or the ATM Agreement may cause the trading price of our common stock to decline and may result in substantial dilution to the interests of other holders of our common stock. The sale of a substantial number of shares of our common stock, including under the Shelf Registration Statement or the ATM Agreement, or anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to sell equity or equity- related securities. We may become involved in securities class action litigation that could divert management' s attention and harm our business. The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biotechnology and biopharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a

company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have in the past experienced significant stock price volatility. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management' s attention and resources, which could adversely affect our business. Future sales of our common stock may cause our stock price to decline and may make it difficult for us to raise additional capital or for you to sell your shares. Sales of substantial amounts of our common stock, or the availability of such common stock for sale, could adversely affect the prevailing market prices for our common stock. If this occurs and continues, it could impair our ability to raise additional capital through the sale of securities if we should desire to do so. In addition, it may be difficult, or even impossible, to find a buyer for shares of our common stock. We have also registered all common stock that we may issue under our current employee benefits plans. As a result, these shares can be freely sold in the public market upon issuance, subject to the terms of the underlying agreements governing the grants and the restrictions of the securities laws. In addition, our directors and officers may in the future establish programmed selling plans under Rule 10b5- 1 of the Exchange Act, for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital. If our estimates or judgments relating to our critical accounting policies are based on assumptions that change or prove to be incorrect, our results of operation could fall below the expectations of securities analysts and investors, resulting in a decline in the market price of our common stock. The preparation of financial statements in conformity with U. S. generally accepted accounting principles (U. S. GAAP) requires management to make estimates and assumptions that affect the amounts reported in our financial statements and accompanying notes. We base our estimates on historical experience and estimates and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets, liabilities, equity, revenue and expenses that are not readily apparent from other sources. For example, as of December 31, ~~2023~~ **2024** , we performed a qualitative impairment assessment of goodwill and indefinite- lived intangible assets which included an evaluation of changes in industry, market, and macroeconomic conditions as well as consideration of our financial performance and any significant trends. If we experience a sustained decline in our stock price or other material changes in the significant assumptions that affect the determination of the fair value of our single reporting unit, it may result in a goodwill and / or intangible asset impairment charge in future periods, and such charge may be material. If our assumptions underlying our estimates and judgments relating to our critical accounting policies change or if actual circumstances differ from our assumptions, estimates or judgments, our operating results may be adversely affected and could fall below the expectations of securities analysts and investors, resulting in a decline in the market price of our common stock. We are a " smaller reporting company " and may take advantage of certain scaled disclosures available to us. We cannot be certain if the reduced reporting requirements applicable to smaller reporting companies will make our common stock less attractive to investors. We are a " smaller reporting company " as defined in the Exchange Act. As a smaller reporting company, we are permitted to comply with scaled disclosure obligations in our SEC filings as compared to other issuers who are not smaller reporting companies, including with respect to disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We have elected to adopt the accommodations available to smaller reporting companies. Until we cease to be a smaller reporting company, the scaled disclosure in our SEC filings will result in less information about our company being available than for public companies that are not smaller reporting companies. We will be able to take advantage of these scaled disclosures for so long as our voting and non- voting common stock held by non- affiliates is less than $ 250 million measured on the last business day of our second fiscal quarter, or (ii) our annual revenue is less than $ 100 million during the most recently completed fiscal year and the market value of our voting and non- voting common stock held by non- affiliates is less than $ 700 million as measured on the last business day of our second fiscal quarter. We cannot predict if investors will find our common stock less attractive because we will rely on certain scaled disclosures that are available to smaller reporting companies. 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. Anti- takeover provisions in our charter documents and under Delaware law may make an acquisition of us more complicated and the removal and replacement of our directors and management more difficult. Our restated certificate of incorporation and amended and restated bylaws contain provisions that may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock or adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. These provisions may also make it difficult for stockholders to remove and replace our board of directors and management. These provisions: • establish that members of ~~the~~ **our** board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least a majority of our capital stock; • authorize the issuance of " blank check " preferred stock that could be issued by our board of directors in a discriminatory fashion designed to increase the number of outstanding shares and prevent or delay a takeover attempt; • limit who may call a special meeting of stockholders; • establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; • prohibit our stockholders from making certain changes to our restated certificate of incorporation or amended and restated bylaws except with 66- 2 / 3 % stockholder approval; and • provide for a classified board of directors with staggered terms. We also may be subject to provisions of the Delaware corporation law that, in general, prohibit any business combination with a beneficial owner of 15 % or more of our common stock for three years unless the holder' s acquisition of our stock was approved in advance by our board of directors. Although we believe these provisions collectively provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In any event, these provisions may delay or prevent a third party from acquiring us. Any such delay or prevention could cause the market price of our common stock to decline.