MEDICINOVA INC
Form 10-K
February 13, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2017

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from. to

Commission file number: 001-33185

MEDICINOVA, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization)	33-0927979 (I.R.S. Employer Identification No.)
4275 Executive Square, Suite 300, La Jolla, CA (Address of Principal Executive Offices)	92037 (Zip Code)

(858) 373-1500

(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
Emerging growth company	

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes No

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $172,754,300 based on the closing price of the registrant's common stock on The NASDAQ Global Market of $5.26 per share on June 30, 2017. Shares of common stock held by each executive officer and director and each affiliated entity has been excluded from this calculation. This determination of affiliate status may not be conclusive for other purposes.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of February 12, 2018 was 40,928,546.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2018 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K.

MEDICINOVA, INC.

FORM 10-K—ANNUAL REPORT

For the Fiscal Year Ended December 31, 2017

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The MediciNova logo is a registered trademark of MediciNova, Inc. All other product and company names are registered trademarks or trademarks of their respective companies.

PART I

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K includes forward-looking statements that involve a number of risks and uncertainties, many of which are beyond our control. The forward-looking statements are contained principally in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” but are also contained elsewhere in this report. Forward-looking statements include all statements that are not historical facts and, in some cases, can be identified by terms such as "believe," "may," "will," "estimate," "continue," "anticipate," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would" or the negative version of these words and similar expressions.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including those described in "Risk Factors" and elsewhere in this report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our beliefs and assumptions only as of the date of this report. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. You should read this report completely and with the understanding that our actual future results may be materially different from what we expect.

The following factors are among those that may cause actual results to differ materially from our forward-looking statements:

- Inability to raise additional capital if needed;
- Inability to generate revenues from product sales to continue business operations;
- Inability to develop and commercialize our product candidates;
- Failure or delay in completing clinical trials or obtaining FDA or foreign regulatory approval for our product candidates in a timely manner;
- Unsuccessful clinical trials stemming from clinical trial designs, failure to enroll a sufficient number of patients, undesirable side effects and other safety concerns;
- Inability to demonstrate sufficient efficacy of product candidates;
- Reliance on the success of our MN-166 (ibudilast) and MN-001 (tipelukast) product candidates;
- Delays in commencement or completion of clinical trials or suspension or termination of clinical trials;
- Loss of our licensed rights to develop and commercialize a product candidate as a result of the termination of the underlying licensing agreement;
- Competitors may develop products rendering our product candidates obsolete and noncompetitive;
- Inability to successfully attract partners and enter into collaborations on acceptable terms;
- Dependence on third parties to conduct clinical trials and to manufacture product candidates;
- Dependence on third parties to market and distribute products;
- Our product candidates, if approved, may not gain market acceptance or obtain adequate coverage for third party reimbursement;
- Disputes or other developments concerning our intellectual property rights;
- Actual and anticipated fluctuations in our quarterly or annual operating results;
- Price and volume fluctuations in the overall stock markets;
- Litigation or public concern about the safety of our potential products;

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- International trade or foreign exchange restrictions, increased tariffs, foreign currency exchange;
- High quality material for our products may become difficult to obtain or expensive;
- Strict government regulations on our business;
- Regulations governing the production or marketing of our product candidates;
- Loss of, or inability to attract, key personnel; and
- Economic, political, foreign exchange and other risks associated with international operations.

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Item 1. Business

Overview

We are a biopharmaceutical company focused on acquiring and developing novel, small molecule therapeutics for the treatment of serious diseases with unmet medical needs and a commercial focus on the United States market. Our current strategy is to focus our development activities on MN-166 (ibudilast) for neurological disorders such as progressive multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), glioblastoma, and substance dependence and addiction (e.g., methamphetamine dependence, opioid dependence, and alcohol dependence), and MN-001 (tipelukast) for fibrotic diseases such as nonalcoholic steatohepatitis (NASH) and 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 currently in development for several different neurological 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). The progressive MS trial 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 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).

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 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.

We have collaborated with Massachusetts General Hospital (MGH) to conduct a clinical trial to study the effects of MN-166 (ibudilast) on reducing brain microglial activation in ALS subjects which can be monitored by a biomarker. This ongoing clinical trial, which we refer to as the ALS / Biomarker study, will also evaluate several clinical outcomes.

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) has funded a Phase 2 clinical trial studying the use of MN-166 (ibudilast) for the treatment of

methamphetamine addiction. In collaboration with UCLA, this clinical trial commenced in 2013 and enrollment was completed in September 2017. We expect results of this trial during the first quarter of 2018. 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.

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 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 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.

•Glioblastoma: We are planning to initiate 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. Results were presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting.

MN-001 (tipelukast) is currently in development for fibrotic diseases including nonalcoholic steatohepatitis (NASH) and idiopathic pulmonary fibrosis (IPF), which are described below.

•Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (NAFLD): A clinical trial is currently ongoing to investigate MN-001 (tipelukast) for the treatment of hypertriglyceridemia in NASH and NAFLD patients. 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.

•Idiopathic Pulmonary Fibrosis (IPF): A Phase 2 clinical trial of MN-001 (tipelukast) to treat moderate to severe IPF is currently enrolling patients. In 2014, we 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 completed a Phase 2 clinical trial of MN-221 for the treatment of acute exacerbations of asthma treated in the emergency room and conducted an End-of-Phase 2 meeting with the United States Food and Drug Administration (FDA) in October 2012. In that meeting, the FDA identified the risk/benefit profile of MN-221 as a focal point for

further development and advised that a clinical outcome, such as a reduction in hospitalizations, would need to be a pivotal trial primary endpoint. We believe the appropriate clinical development for MN-221 will involve conducting dose regimen and acute exacerbations of asthma trial design optimization studies prior to commencing pivotal trials. We are working to identify a partner for financial support before further clinical development is commenced.

We have acquired licenses to MN-166, MN-001, MN-221, and MN-029 for the development of these product candidates. We have pursued development of these product candidates in various indications including progressive MS, ALS, various addictions, NASH, 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. In addition to providing drug supply and regulatory support, we are funding portions of the consortium-sponsored trials. For example, we contributed financially to the Secondary and Primary Progressive Ibudilast NeuroNEXT Trial in Multiple Sclerosis (SPRINT-MS) Phase 2b clinical trial of MN-166 (ibudilast) for the treatment of progressive MS, which was primarily funded by the NIH. In addition, we contributed financially to the clinical trial of MN-166 (ibudilast) for the treatment of ALS as well as the ongoing ALS / Biomarker study. 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 diseases such as NASH and IPF.
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 late-stage product development and successfully commercialize our products.
We develop and maintain relationships with pharmaceutical companies that are therapeutic category leaders. Upon completion of proof-of-concept Phase 2 clinical trials, we intend to discuss strategic alliances with leading pharmaceutical companies who seek late-stage product candidates, such as MN-166, MN-001, MN-221 and MN-029, which could support further 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 Investigational New Drug (INDs) 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)

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 primary progressive and secondary progressive MS, ALS, glioblastoma, and substance dependence. 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 10 years of marketing exclusivity if it is approved for ALS in Europe.

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, and for the treatment of drug addiction or dependence.

Primary and Secondary Progressive Multiple Sclerosis: MS is a complex disease with predominantly unknown etiology and affects approximately 2.3 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 most 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. 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. 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. 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. Life expectancy of an ALS patient is usually two to five years. According to the ALS Association, there are approximately 20,000 ALS patients in the United States and approximately 6,000 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 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) for a new patent which covers MN-166 (ibudilast) for the

treatment of amyotrophic lateral sclerosis (ALS). 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 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 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. This ongoing clinical trial, which we refer to as the ALS / Biomarker study, will also evaluate safety and tolerability as well as several clinical outcomes including ALS functional rating scale (ALSFRS-R), slow vital capacity (SVC), and muscle strength measured by hand-held dynamometry (HHD).

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) 2016 National Survey on Drug Use and Health, there are approximately 684,000 people aged 12 or older with methamphetamine use disorder (includes those with dependence or abuse) in the United States. According to the Rand Corporation, the estimate of the economic burden in the United States of methamphetamine use, based on the most recent year for which data are available, 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. Enrollment in this trial was completed in September 2017 and we expect results of this trial during the first quarter of 2018. 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. 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 2016 National Survey on Drug Use and Health, there are approximately 1.8 million people aged 12 or older with pain reliever use disorder (includes those with dependence or abuse) and approximately 626,000 people aged 12 or older with heroin use disorder (includes those with dependence or abuse) 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 (Knopf, 2012). The economic costs of nonmedical use of prescription opioids in the United States. in 2006 (Hansen et al., 2011), the most recent year for which data is available, was estimated to total more than $50 billion annually, with lost productivity and crime accounting for 94% of the total economic burden. 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 NYSPI previously completed a NIDA-funded, double-blind, randomized, 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 dependency. 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 2016 National Survey on Drug Use and Health, there are approximately 15.1 million people aged 12 or older with alcohol use disorder (includes those with dependence or abuse) in the United States. The Centers for Disease Control and Prevention (CDC) reports that excessive alcohol use cost the United States $249 billion in 2010, the latest year for which complete data are available. Currently, medicines approved by the FDA to treat alcohol dependence include Antabuse®, Vivitrol®, Campral® and Revia®. However, the search for a safe and effective drug remains elusive due to limited success of these FDA-approved compounds (Witkiewitz et al., 2012). In a non-clinical trial (Bell et al., 2013), MN-166 (ibudilast) was examined in rats and mice and was found to reduce alcohol drinking in alcohol-preferring P rats and high-alcohol drinking (HAD1) rats by 50%, and in mice made dependent on alcohol at doses which had no effect on non-dependent mice. Investigators at UCLA received funding from the NIAAA to conduct a study to evaluate MN-166 (ibudilast) in a randomized, double-blind, placebo-controlled within-subject crossover design to determine the safety, tolerability and initial human laboratory efficacy of MN-166 (ibudilast) in a sample of 24 non-treatment seeking individuals with either alcohol abuse or dependence. The study was initiated in early 2014 and completed enrollment of 24 subjects in June 2015. Results of the alcohol dependence study were presented at the American College of Neuropsychopharmacology (ACNP)'s 54th Annual Meeting in December 2015. MN-166 (ibudilast), but not placebo, significantly decreased basal, daily alcohol craving over the course of the study ($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.

Glioblastoma: Malignant primary brain tumors represent the most frequent cause of cancer death in children. According to the American Association of Neurological Surgeons, glioblastoma (GBM) is an aggressive, extremely lethal form of brain malignancy that develops from glial cells (astrocytes and oligodendrocytes) and rapidly grows and commonly spreads into nearby brain tissue. GBM is classified as Grade IV, the highest grade, in the World Health Organization (WHO) brain tumor grading system. The American Brain Tumor Association reports that GBM represents 15% of all primary brain tumors and 55% of all gliomas and has the highest number of cases of all malignant tumors, with an estimated 12,390 new cases predicted for 2017. Despite decades of advancements in neuroimaging, neurosurgery, chemotherapy, and radiation therapy, only modest improvements have been achieved and the prognosis has not improved for individuals diagnosed with GBM. Median survival of GBM patients is 14.6 months. 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 GBM which were presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting. Results of the GBM mouse model study showed that median survival was higher in the group that received combination treatment with MN-166 (ibudilast) plus temozolomide (TMZ) compared to the group that received TMZ alone.

MN-221 (bedoradrine)

MN-221 (bedoradrine) is a novel, highly selective $ß_2$-adrenergic receptor agonist which has been developed for the treatment of acute exacerbations of asthma. We licensed MN-221 from Kissei Pharmaceutical Co., Ltd. (Kissei) in February 2004. 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 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 to have a high affinity for the $ß_2$-adrenergic receptor, found primarily in the lungs, and a much lower affinity for the $ß_1$-adrenergic receptor found primarily in cardiac tissue. MN-221's improved delivery to the lungs and its cardiac safety profile may 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 United States National Center for Health Statistics, there were 1.75 million emergency department visits, 439,000 hospitalizations, and

3,404 deaths due to asthma in 2010. According to the United States National Heart, Lung and Blood Institute, the direct costs associated with hospital care due to asthma were estimated at $5.5 billion in the United States in 2010.

We completed a Phase 2b randomized, double-blind, placebo-controlled clinical trial (N=175) evaluating MN-221 in patients with acute exacerbations of asthma in the emergency department setting. MN-221 did not statistically meet the primary endpoint, improvement in FEV_1 (Forced Expiratory Volume in One Second) compared to placebo. However, MN-221 treatment demonstrated statistically significant improvements in endpoints associated with Dyspnea Index scores. MN-221 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 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 as a focal point for further development and advised that a clinical outcome, such as a reduction in hospitalizations, would need to be a pivotal trial primary endpoint. We have decided that any future MN-221 development will be designed based on the feedback received from the FDA and that any future MN-221 clinical trial development for asthma will be partner-dependent from a funding perspective.

MN-001 (tipelukast)

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 MN-001 (tipelukast)’s inhibitory effect 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 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 exposed to more than 600 subjects and is considered generally safe and well-tolerated.

Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (NAFLD): Nonalcoholic steatohepatitis (NASH) is 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 3-12%, and an additional 30-40% of adult Americans 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 treatment for NASH.

We completed a pre-clinical study evaluating MN-001 (tipelukast)’s potential clinical efficacy 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, 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 MN-001 (tipelukast)'s anti-fibrotic properties. 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 provide 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 two different Phase 2 clinical trial protocols for MN-001 (tipelukast) for the treatment of NASH in the United States. A Phase 2 clinical trial is currently ongoing to investigate MN-001 (tipelukast) for the treatment of hypertriglyceridemia in NASH patients and NAFLD patients. The FDA has granted Fast Track designation to MN-001 (tipelukast) for the treatment of patients with NASH with fibrosis.

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 Pulmonary Fibrosis Foundation, IPF affects between 132,000 – 200,000 people in the United States, and an estimated 50,000 new cases are diagnosed annually. The prognosis for IPF is poor with a median survival of only two to three years following diagnosis and more than two-thirds of IPF patients die within five years.

We completed a pre-clinical study evaluating MN-001 (tipelukast)'s potential clinical efficacy 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 Vehicle 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 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 moderate to severe IPF in the United States. A Phase 2 clinical trial of MN-001 (tipelukast) to treat moderate to severe IPF is currently ongoing at Penn State. 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)

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 from Angiogene Pharmaceuticals, Ltd. (Angiogene) in 2002.

Several preclinical pharmacology studies have assessed the mechanism of action and anti-tumor activity of MN-029 in vivo in rodent models of breast adenocarcinoma, colon carcinoma, lung carcinoma and KHT sarcoma. In these studies, MN-029 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 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 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 given every three weeks in 34 subjects with refractory cancer. The MTD was determined to be 180 mg/m^2 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 were 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 had a desired vascular effect in seven of 11 patients that were administered drug at dose levels of ≥120 mg/m^2. 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 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 could receive additional cycles. All 20 subjects reported at least one AE related to study drug. The most common AEs considered related to 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 study drug. Consistent with the previous Phase 1 trial, MN-029 up to dose levels of 180 mg/m^2 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 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. We plan to pursue further development of MN-029 for the treatment of solid tumors.

Table 1 Product Candidates and Programs—MN-166 (ibudilast)

Indication	Clinical Study	Principal Investigator /Institution /Funding Agency(s)	Status
Primary Progressive and Secondary Progressive Multiple	A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability and Activity of Ibudilast	Robert J. Fox, M.D., M.S., FAAN Cleveland Clinic	Completed

Sclerosis	(MN-166) in Subjects with Progressive Multiple Sclerosis	National Institute on Neurological Diseases and Stroke MediciNova, Inc.

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)	Benjamin R. Brooks, M.D. Carolinas HealthCare System Neurosciences Institute MediciNova, Inc.	Completed
	A Biomarker Study to Evaluate MN-166 (Ibudilast) in Subjects With Amyotrophic Literal Sclerosis (ALS)		
ALS / Biomarker		Nazem Atassi, M.D., MMSc Massachusetts General Hospital MediciNova, Inc.	Ongoing
Substance Dependence / Addiction:			
Methamphetamine Dependence	Randomized Trial of Ibudilast for Methamphetamine Dependence	Keith Heinzerling, M.D., MPH UCLA National Institute on Drug Abuse	Ongoing
Methamphetamine Dependence / Biomarker	Effect of Ibudilast on Neuroinflammation in Methamphetamine Users	William Hoffman, M.D., Ph.D. Oregon Health & Science Univ.	Ongoing

Opioid Dependence	Effects of Ibudilast (MN-166), a Glial Activation Inhibitor, on Oxycodone Self-Administration in Opioid Abusers	Sandra D. Comer, Ph.D. Columbia University/NYSPI National Institute on Drug Abuse MediciNova, Inc.	Completed
Alcohol Dependence	Development of Ibudilast (MN-166) as a Novel Treatment for Alcoholism	Lara Ray, Ph.D. UCLA National Institute on Alcohol Abuse and Alcoholism	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 sourced and imported delayed-release ibudilast capsules, marketed in Japan as Pinatos®, from Taisho Pharmaceutical Co., Ltd. (Taisho).

Pursuant to the terms of our license agreement with Kissei for MN-221, Kissei has the exclusive right to manufacture the commercial supply of the API for MN-221. If we enter into a supply agreement with Kissei, we will purchase from Kissei all API that we require for the commercial supply of MN-221, if this product candidate is approved for commercial sale by the FDA or other regulatory authorities.

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 licensed rights to one issued U.S. patent and 19 issued foreign patents. In addition to these licensed rights, we hold 24 issued U.S. patents and have filed 6 additional U.S. patent applications. We also hold 36

issued foreign patents and 44 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 product candidates.

MN-166 (ibudilast)

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 First Section of the Tokyo Stock Exchange. 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-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 is set to expire on August 10, 2018. Corresponding method of use patents in certain foreign countries are set to expire 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 seven issued U.S. patents and five pending U.S. patent applications as well as 22 issued foreign patents and seven 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 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 patent which covers the use of MN-166 (ibudilast) for the treatment of drug addiction or drug dependence or withdrawal syndrome in the United States 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 patent which covers the use of MN-166 (ibudilast) for the treatment of neuropathic pain in the United States and it expires no earlier than December 2025.

MN-221 (bedoradrine)

On February 25, 2004, we entered into an exclusive license agreement with Kissei for the development and commercialization of MN-221. Kissei is a fully integrated Japanese pharmaceutical company and is listed on the Tokyo Stock Exchange. We obtained an exclusive, worldwide (excluding Japan), sub-licensable license to various patent rights and know-how related to MN-221 and other compounds disclosed or included in, or covered by, these patent rights, for all indications. This license includes an exclusive license under one U.S. patent and certain corresponding patents in foreign countries and is sub-licensable upon receipt of the written consent of Kissei. The United States composition of matter patent underlying the license issued on October 17, 2000 and it expired on February 18, 2017. Most of the corresponding composition of matter patents in various other countries also expired on February 18, 2017.

In addition to the licensed patents, we have filed patent applications in the United States and certain foreign countries regarding additional uses and formulations of MN-221. We have been granted a U.S. patent which covers the use of MN-221 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 for the treatment of irritable bowel syndrome and it expires no earlier than April 2031.

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 scientific or commercial reasons upon 100 days' prior written notice to Kissei during the development phase and 180 days' prior written notice to Kissei during the commercialization phase.

The term of the agreement is determined on a country-by-country basis and extends until the expiration of the last Kissei patent (or equivalent) under license to expire or in the event that a valid claim does not exist or, if a valid claim expired more than ten years from the date of first commercial sale, ten years from the date of first commercial sale. In either case, the term of the agreement would not extend for any particular country past the date on which generic competition exists in such country.

Under the license agreement, we have paid Kissei $1.0 million to date, and we are obligated to make payments of up to $17.0 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. Under the terms of a letter agreement we entered into with Kissei in September 2011, we agreed to renegotiate in good faith with Kissei the existing levels of the milestone payment amounts and royalty rates.

MN-001 (tipelukast)

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 includes 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 have been granted 14 U.S. patents covering certain compositions, uses and manufacturing processes associated with MN-001 (tipelukast) and MN-002. Uses covered by these 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.

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 $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.

MN-029 (denibulin)

On June 19, 2002, we entered into an exclusive license agreement with Angiogene for the development and commercialization of the ANG-600 series of compounds. Angiogene is a privately held, British drug discovery company. 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 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 or allowed 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 to expire 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.

General

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 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 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 and 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. Only one drug, mitoxantrone, is approved for the treatment of secondary progressive MS. However, mitoxantrone cannot be used on a long-term basis because of the potential for cardiac toxicity. Only one drug, Ocrevus (ocrelizumab) is approved for the treatment of primary progressive MS. Other programs in clinical development for progressive MS include Novartis's BAF312 (siponimod), Teva's Nerventra (laquinimod), 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. Riluzole and Radicava (edaravone) 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 Cytokinetics, BrainStorm Cell Therapeutics Inc., AB Science, Mallinckrodt, Biogen, Neuraltus Pharmaceuticals, and Amylyx Pharmaceuticals.

MN-166 (ibudilast) for Substance Dependence and Addiction

Our MN-166 (ibudilast) product candidate is also in development for 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' Vivitrol® (naltrexone monthly injection), Orexo's Zubsolv® (buprenorphine and naloxone), BioDelivery Sciences's Bunavail® (buprenorphine and naloxone), Braeburn Pharmaceuticals Inc.'s Probuphine (buprenorphine) implant, and Indivior's Sublocade (buprenorphine extended-release injection). Braeburn Pharmaceuticals is developing an injectable buprenorphine product for the treatment of opioid dependence. Limited non-narcotic drug candidates for opioid withdrawal symptoms exist. Britannia Pharmaceuticals Limited's BritLofex® (Lofexidine), an a_2 adrenergic receptor agonist like clonidine which may have somewhat less orthostatic hypotension limitations, was licensed to US WorldMeds LLC for development in the United States for opioid withdrawal symptoms. There are no pharmaceuticals currently approved for the treatment of methamphetamine addiction. Current treatments for alcohol dependence include Antabuse® (disulfiram), Vivitrol® (naltrexone), and generic acamprosate. We are aware of additional compounds in development for the treatment of alcohol dependence at other companies including Indivior.

MN-221 (bedoradrine) for Acute Exacerbations of Asthma

Our MN-221 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 $ß_2$ -adrenergic receptor agonist), inhaled ipratropium (an anticholinergic) and oral or injected corticosteroids. In addition, subcutaneously administered terbutaline (a $ß_2$ -adrenergic receptor agonist) is sometimes used to treat this condition, particularly in pediatric patients.

MN-001 (tipelukast) for Nonalcoholic Steatohepatitis (NASH)

Our MN-001 (tipelukast) product candidate is being developed for the treatment of NASH. There are currently no therapeutic products approved for the treatment of NASH. We are aware of compounds in clinical development for the treatment of NASH at other companies including Intercept Pharmaceuticals, Genfit, Galectin Therapeutics, Gilead Sciences, Allergan (which acquired Tobira Therapeutics), Galmed Pharmaceuticals, Bristol-Myers Squibb, Shire and Conatus Pharmaceuticals.

MN-001 (tipelukast) for Idiopathic Pulmonary Fibrosis (IPF)

Our MN-001 (tipelukast) product candidate is also being developed 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, Biogen and FibroGen.

MN-029 (denibulin) for Solid Tumor Cancer

Our MN-029 product candidate is being 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/or 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, Amgen and Celgene.

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 of 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;
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