MEDICINOVA INC
Form 10-K
March 28, 2013
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2012

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	**33-0927979**
(State or Other Jurisdiction of Incorporation	**(I.R.S. Employer Identification No.)**
or Organization)	
4275 Executive Square, Suite 650, La Jolla, CA	**92037**
(Address of Principal Executive Offices)	**(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:

Series A Participating Preferred Stock Purchase Rights

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

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 [X]

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 [X] 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). [X] 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. [X]

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

Large accelerated filer [ ] Accelerated filer [ ] Non-accelerated filer [ ] Smaller reporting company [X]

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 [X]

The aggregate market value of the registrant s common stock held by non-affiliates of the registrant was approximately $22,014,000 based on the closing price of the registrant s common stock on the Nasdaq Global Market of $1.63 per share on June 29, 2012. Shares of common stock held by each executive officer and director and each person who beneficially owns 10% or more of the outstanding common stock have 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 March 27, 2013 was 18,244,502.

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 2013 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.

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MEDICINOVA, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2012

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PART I

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. Our actual results may differ from those anticipated or expressed in these forward-looking statements as a result of various factors, including those set forth below under the caption Item 1A. Risk Factors, and the differences may be material. Forward-looking statements discuss matters that are not historical facts. Forward-looking statements include discussions regarding our operating strategy, growth strategy, licensing and acquisition strategy, cost savings initiatives, industry and economic conditions, market factors, financial condition, liquidity and capital resources, results of operations, expected progress of the development of our product candidates, potential licensing, collaboration and partnering plans, anticipated trends and challenges in our business and the markets in which we operate, competitive position, intellectual property protection, critical accounting policies and the impact of recent accounting pronouncements. In this report, for example, we make forward-looking statements regarding the potential for our product candidates to receive regulatory approval for one or more indications on a timely basis or at all; the progress and results of pending clinical trials for certain of our product candidates, including any delays in commencing or completing enrollment for our ongoing or planned clinical trials; plans for future clinical trials and regulatory submissions; unexpected adverse side effects or inadequate therapeutic efficacy of certain of our product candidates that could delay or prevent regulatory approval or commercialization or that could result in product liability claims; other difficulties or delays in development, testing, manufacturing and marketing of and obtaining regulatory approval for our product candidates; the scope and validity of patent protection for our product candidates; the market potential for our target markets and our ability to compete; the potential to attract and maintain relationships with one or more strategic partners and terms of any related transactions; intense competition if any of our product candidates are ever commercialized; our ability to realize the anticipated strategic and financial benefits of our acquisition of Avigen, Inc., or Avigen; the potential impact of uncertainties in the credit and capital markets or a future deterioration of these markets on our investment portfolio; and our ability to raise sufficient capital or debt financing when needed, or at all. Such forward-looking statements include statements preceded by, followed by or that otherwise include the words may, might, will, intend, should, could, can, would, expect, believe, estimate, anticipate, predict, potential, plan or similar words. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. You should not rely unduly on these forward-looking statements, which speak only as of the date on which they are made. We undertake no obligation to revise or update publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

Item 1. Business

Overview

We are a development stage biopharmaceutical company focused on developing novel, small molecule therapeutics for the treatment of serious diseases with unmet medical needs with a commercial focus on the U.S. market. We are currently focusing our development activities on MN-166, an ibudilast-based drug candidate for the treatment of neurological disorders, and obtaining additional funding to advance clinical trial development of MN-221, a novel, highly selective $ß_2$ -adrenergic receptor agonist being developed for the treatment of acute exacerbations of asthma and chronic obstructive pulmonary disease, or COPD.

We completed a Phase 2 clinical trial of MN-166 for the treatment of multiple sclerosis (MS) in 2008. Positive safety and neuroprotective efficacy indicators were observed in that trial and we are seeking collaborations to resume a clinical development program for the treatment of progressive multiple sclerosis. In the area of drug dependence, in 2010, investigators at Columbia University and the New York State Psychiatric Institute completed a double blinded, placebo controlled, Phase 1b/2a opioid withdrawal clinical trial that was

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funded by the National Institute on Drug Abuse, or NIDA. Investigators at Columbia and the New York State Psychiatric Institute recently commenced a NIDA funded, double blinded, placebo controlled, Phase 2a clinical trial to determine the effect of MN-166 for the withdrawal treatment of patients addicted to prescription opioids or heroin. This trial is expected to proceed through mid-2014 and, assuming a positive outcome, is expected to be followed by a Phase 2 trial for opioid dependence. Investigators at UCLA recently completed enrollment of a Phase 1b NIDA funded clinical trial of MN-166 in methamphetamine-dependent volunteers. We expect results from the trial to be announced in the second quarter of 2013. In September 2012 we announced approval and funding by NIDA of a Phase 2 clinical trial studying the use of MN-166 for the treatment of methamphetamine addiction. In collaboration with UCLA, this clinical trial will build on the UCLA Phase 1b trial. A Phase 2 investigator sponsored clinical trial of MN-166 in the treatment of chronic medication overuse headache (MOH) pain has been initiated by a headache and pain specialist in Australia and is expected to be completed by mid-2013. We have provided supplies of MN-166 and safety and regulatory support for the drug dependence trials and MOH trial. We intend to complement additional grant supported clinical development with targeted MediciNova support.

We completed a Phase 2 clinical trial of MN-221 for the treatment of acute exacerbations of asthma treated in the emergency room in 2012 and conducted an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, or FDA, in October 2012. We plan to conduct the MN-221 program according to the feedback received from the FDA following the End-of-Phase 2 meeting. 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. Previously completed Phase 2 studies have evaluated the potential for MN-221 to reduce hospitalizations due to acute exacerbations of asthma. 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. Currently, we are working to address the manufacturing requirements before further clinical development is commenced. In the area of COPD exacerbations, we have completed two Phase 1b clinical trials of MN-221. We have determined that any future MN-221 clinical trial development will be partner-dependent from a funding perspective.

Including MN-166 and MN-221 and our other product development programs, we have acquired licenses to eight compounds for the development of ten product candidates which include clinical development for the treatment of acute exacerbations of asthma, MS and other central nervous system (CNS) disorders, bronchial asthma, interstitial cystitis (IC), solid tumor cancers, generalized anxiety disorders/insomnia, preterm labor and urinary incontinence.

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. Our focus is on the U.S. market. Key elements of our strategy are as follows:

Pursue the development of MN166 for multiple potential indications primarily through non-dilutive financings. We intend to advance our diverse MN-166 (ibudilast) program through a combination of investigator sponsored trials and trials funded through government grants or private and public grants. In addition to providing drug supply and safety regulatory support, we may fund portions of the investigator or consortium sponsored trials. For example, we intend to increase our financial participation in the Phase 2 clinical trial of MN-166 for the treatment of methamphetamine addiction that investigators at UCLA will conduct primarily with funding from NIDA. We intend to enter into additional strategic alliances to support further clinical development of MN-166.

Strategically partner 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 therapeutic area leaders. Upon completion of proof-of-concept Phase

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2 clinical trials, we intend to enter into strategic alliances with leading pharmaceutical companies who seek late stage product candidates, such as MN-221, to support further clinical development and product commercialization.

Product Development 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 U.S. We utilize the existing data in preparing Investigational New Drug Applications, or INDs, or their foreign equivalents, and in designing and implementing additional preclinical or clinical trials to advance the regulatory approval process in the U.S. or abroad.

Following are the details of our product development programs:

MN-166 (Ibudilast)

MN-166 is a novel, first-in-class, non-opioid drug for the treatment of several indications with potentially large addressable patient populations including drug addiction, progressive MS and pain. MN-166 is a relatively potent and selective inhibitor of macrophage migration inhibitory factor (MIF) and phosphodiesterases (PDEs) -4 and -10. It is a first-in-class, orally bioavailable small molecule, glial attenuator that suppresses pro-inflammatory cytokines IL-1ß, TNF-a, and IL-6, and may increase the release of the anti-inflammatory cytokine IL-10 and neuroprotective growth factors (e.g. GDNF). It has additionally been shown to be a toll-like receptor 4 (TLR4) functional antagonist, which property may contribute to its attenuation of neuroinflammation. While considered a New Molecular Entity, or NME, in the U.S. and Europe, ibudilast was first approved in Japan more than 20 years ago for the treatment of cerebrovascular disorders and bronchial asthma. Ibudilast has been prescribed to over three million patients and has an established post-marketing safety profile as reported in nearly 15,000 patients studied at the prescribed doses in Japan.

Based on our research, we have filed patent applications for multiple uses of MN-166 (ibudilast) for the treatment of neurological conditions, as well as patents on analogs which we believe have the potential to be effective second generation molecules. Some of the patent estate has received allowance in the U.S. and foreign countries.

Opioid withdrawal: According to the Substance Abuse and Mental Health Services Administration s (SAMHSA) 2011 National Survey on Drug Use and Health, there are approximately 1.4 million people with nonmedical pain reliever dependence and approximately 369,000 people with heroin dependence in the U.S. The economic costs of nonmedical use of prescription opioids in the U.S. was estimated at $53.4 billion in 2006, according to a study published in The Clinical Journal of Pain. Most of the medications currently approved by the FDA for the treatment of opioid dependence are opioid agonists which carry the risk of secondary dependence or abuse and have opioid-related safety risks. Accordingly, there is an unmet need for a safe, effective, non-addictive therapy for the treatment of opioid withdrawal and dependence. In 2010, investigators at Columbia University and New York State Psychiatric Institute completed a Phase 1b/2a double blinded placebo-controlled clinical trial of MN-166 for the treatment of opioid withdrawal and analgesia, or OWA, in which 30 patients were enrolled. The trial was funded by NIDA. Investigators at Columbia University and New York State Psychiatric Institute recently commenced an investigator led double-blinded,

placebo-controlled, Phase 2a clinical trial of MN-166 for the treatment of addictions to prescription opioids or heroin in which 24 patients were enrolled. This trial is expected to proceed through mid 2014 and, assuming a positive outcome, is expected

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to be followed by a Phase 2 trial for opioid dependence. MN-166 and analogs have been shown in preclinical models of opioid (morphine or oxycodone) withdrawal to reduce significantly patient withdrawal symptoms. MN-166 and analogs are differentiated from other drug candidates in clinical trials that may demonstrate similar effects, in that MN-166 and analogs are not narcotics and do not, themselves, provide reward or reinforcement in behavioral models of dependence. Thus, while current therapies involve substitution of one opioid for another (e.g. methadone for heroin), MN-166 represents a novel non-opioid approach for the treatment of opioid withdrawal and dependence. Results from the recently-completed OWA trial indicated dose-related attenuation of the opioid withdrawal syndrome relative to the placebo control for the 80mg dose of MN-166, measured using the Subjective Opioid Withdrawal Scale (SOWS). SOWS is a rating scale for measuring the signs and symptoms of opiate withdrawal. SOWS contains 16 symptoms that patients rate for intensity on a scale of 0 (not at all) to 4 (extremely). The trial also observed an enhanced opioid analgesia relative to the placebo control for the 80mg dose of MN-166, measured using the McGill Pain Questionnaire. Other measures of withdrawal (Clinicians Opioid Withdrawal Scale) or analgesia (quantitative time endpoints for cold pressor test) did not demonstrate a dose-related response.

Methamphetamine addiction: Methamphetamine is a highly addictive stimulant that is closely related to amphetamine. It is long lasting and toxic to dopamine nerve terminals in the central nervous system. It is a white, odorless, bitter-tasting powder taken orally or by snorting or injecting, or a rock crystal that is heated and smoked. Methamphetamine increases wakefulness and physical activity, produces rapid heart rate, irregular heartbeat and increased blood pressure and body temperature. Long-term use can lead to memory loss, aggression, psychotic behavior, heart damage, malnutrition and severe dental problems. All users, but particularly those who inject the drug, risk infectious diseases such as HIV/AIDS and hepatitis. According to the Substance Abuse and Mental Health Services Administration s (SAMHSA) 2011 National Survey on Drug Use and Health, there are approximately 439,000 methamphetamine abusers in the U.S. An independent study conducted by the Rand Corporation estimated the economic burden of methamphetamine use in the U.S. at $23.4 billion in 2005. There are no medications currently approved by the FDA for the treatment of methamphetamine dependence. We, in collaboration with NIDA, have demonstrated MN-166 (ibudilast) s utility in methamphetamine relapse in animals. As a result of the animal studies, NIDA funded an exploratory Phase 1b methamphetamine interaction clinical trial of MN-166 led by investigators at UCLA. This trial has now completed enrollment with results expected to be publicly released in the second quarter of 2013. In September 2012 we announced approval and funding by NIDA of a Phase 2 clinical trial studying the use of MN-166 for the treatment of methamphetamine addiction. Investigators at UCLA will lead the planned Phase 2 trial with our participation.

We recently received Fast Track designation from the FDA for MN-166 (ibudilast) for the treatment of methamphetamine dependence. Fast Track 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.

Progressive Multiple Sclerosis (MS): MS is an inflammatory disease of the CNS in which the body s immune system attacks the protective sheath surrounding nerve fibers. According to the National Multiple Sclerosis Society, MS affects approximately 400,000 people in the U.S. and approximately 2.5 million people worldwide. The most obvious effect of MS is its destruction of nerve fibers leading to the loss of muscle control. However, MS also affects multiple CNS functions. Currently, there is no known cure for the disease. According to the National Multiple Sclerosis Society, relapsing-remitting MS, or RRMS, is the most common type of the disease, and 85 percent of people with MS are initially diagnosed with RRMS. A majority of RRMS patients progress to secondary progressive MS (SPMS). The most severe type of MS, primary progressive MS (PPMS), represents about 10% of all MS. According to sales data included in most recent annual reports of leading MS drug companies, including Biogen Idec Inc., Merck Serono S.A., Reva Pharmaceutical Industries Ltd., Bayer AG, Novartis AG and Sanofi, worldwide sales of drugs to treat MS exceeded $13.9 billion in 2012.

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Based on its anti-inflammatory activity and safety profile, MN-166 was evaluated for potential activity in MS in two pilot clinical trials sponsored by academic investigators in Japan. In the first pilot trial, the average relapse rate was reduced, there was no significant change in the mean Expanded Disability Status Score, or EDSS, a measure of MS drug efficacy and disease progression, and no side effects of MN-166 were reported. In a second pilot trial, MN-166 tended to normalize the levels of several chemical mediators of inflammation, including TNF-a and interferon gamma.

We completed a two-year Phase 2 multi-center, randomized, double-blind, placebo-controlled clinical trial of MN-166 for the treatment of patients with relapsing MS in April 2008. This clinical trial involved 297 patients with relapsing MS in several countries in Eastern Europe. Patients received either 30 mg of MN-166 per day, 60 mg of MN-166 per day or a placebo. In the second year of the study, all patients received active drugs. Patients who received 30 or 60 mg of MN-166 per day during the first year of the study remained on the assigned dose for the second 12 months of the study; patients who received placebo during the first 12 months of the study were randomized to receive either 30 or 60 mg of MN-166 per day (double-blind maintained) during the second 12 months of the study. Clinical and radiological outcomes were evaluated. MN-166 treatment resulted in positive findings on three independent measures indicative of a potential disease-progression modifying effect. First, sustained disability progression was significantly less likely (by approximately 50 percent) in those patients receiving MN-166 at either 30 or 60 mg per day for 24 months than in those patients receiving the drug for 12 months (p=0.026). Sustained disability progression was measured as a greater than or equal to 1.0 point increase from baseline in the EDSS score for four consecutive months. Second, the significant reduction in brain volume loss (p=0.035), as measured by cranial MRI scans, observed after 12 months in patients treated with 60 mg per day of MN-166 compared to placebo was again demonstrated in year two of the study. Brain volume loss was significantly less (p=0.030) in patients receiving 60 mg per day of MN-166 for 24 months compared to the other treatment groups. Third, MN-166 treatment at 60 mg per day significantly reduced the relative risk for conversion of new inflammatory lesions identified at month two to PBHs eight months later at month ten by 37 percent (p=0.011); such lesions that remain unchanged for eight months are considered PBHs as compared to transient inflammatory lesions that are more closely associated with relapses. MN-166 treatment at 30 mg per day resulted in a trend toward reducing evolution to PBH (p=0.074). MN-166 was well tolerated at all doses over the two years of this clinical trial, with the most common adverse events possibly related to MN-166 involving mild, transient gastrointestinal disturbances and depression. Of the 297 patients enrolled in this clinical trial, 245 patients completed the full two years of treatment. In September 2008, data from this completed two-year clinical trial was presented at the World Congress for Treatment and Research in MS.

Based on some of our prior Phase 2 trial outcomes and opinions provided by multiple sclerosis experts and advisors, MN-166 may be well positioned as a therapy for progressive MS. It is our intent to advance MN-166 into a Phase 2 proof-of-concept trial for the treatment of progressive MS and to fund that development via strategic collaborations or other means of raising additional capital. There can be no assurance that we will be able to successfully secure such strategic collaborations or fundraising activities.

Neuropathic pain: Neuropathic pain is a complex chronic pain in which the nerve fibers are damaged or dysfunctional. Although precise estimates of the prevalence of neuropathic pain are not available, there are approximately 3 million people with painful diabetic neuropathy in the U.S., according to a study published in the Clinical Journal of Pain. Effective treatment of chronic neuropathic pain remains an unmet and serious need. Until recently, conceptualization of neuropathic pain had been neuronically-based with most drugs approved or in development being related to neuronal targets. This approach has been revised significantly in light of recognition of the profound role glial activation has in creating and sustaining enhanced pain states. Accordingly, a pharmacotherapy that is orally administered daily and directed at attenuating glial activation may offer pain relief as a stand-alone medication or as an additive to existing drug therapies and would have significant utility. MN0166 (ibudilast) is a chronic pain drug candidate that may meet all of these criteria. Microphage migration inhibitory factor (MIF) activity and glial activation in the brain and spinal cord contribute to the establishment and amplification of the chronic pain state. MN-166 (Ibudilast) has demonstrated activity in preclinical models of neuropathic pain and may be effective in a wide range of neuropathic pain syndromes including neuropathy,

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post-herpetic neuralgia, HIV neuropathy, radiculopathy, spinal cord injury and chemotherapy-induced neuropathy. While ibudilast was initially developed as a non-selective phosphodiesterase (PDE) inhibitor for the treatment of bronchial asthma, its efficacy in some neuropathic pain models appears to be independent of this activity and yet still linked to glial attenuation. Ibudilast has advanced through multiple Phase 1 and 2a clinical trials in both healthy volunteers and patients for neuropathic pain, inclusive of a Phase 1b/2a clinical trial in diabetic neuropathic pain. The program, under current FDA standards, is able to enter Phase 2 development for neuropathic pain in the U.S. based on our completed preclinical and clinical development. A Phase 2 investigator sponsored, double-blind, placebo-controlled clinical trial of MN-166 in the treatment of chronic medication overuse headache (MOH) pain in which 40 patients are enrolled has been initiated by a headache and pain specialist in Australia and is expected to be completed by mid-2013.

MN-221 (bedoradrine)

MN-221 is a novel, highly selective ß$_2$ -adrenergic receptor agonist being developed for the treatment of acute exacerbations of asthma and COPD. We licensed MN-221 from Kissei Pharmaceutical Co., Ltd., or Kissei, in February 2004. Preclinical studies conducted *in vitro* and *in vivo* showed MN-221 to be highly selective for the ß$_2$ -adrenergic receptor. In these studies, the ß$_1$ -adrenergic receptor stimulating activity of MN-221 was less than that of other ß$_2$-adrenergic receptor agonists in isolated rat atrium and *in vivo* cardiac function tests in rats, dogs and sheep, thereby suggesting that the stimulating action of older, less selective ß$_2$ -adrenergic receptor agonists on the heart via ß$_1$ -adrenergic receptors may be reduced with MN-221. *Some in vitro* studies also suggested that MN-221 may act as only a partial ß$_1$ -adrenergic receptor agonist in cardiac tissue, while acting as a full ß$_2$ -adrenergic receptor in lung tissue. In addition, a preclinical drug interaction study in dogs completed during 2008 demonstrated that, while each of albuterol and MN-221 induced an increase in heart rate independently, the addition of MN-221 by intravenous administration in combination with inhaled albuterol did not add to the heart rate increase associated with inhaled albuterol alone. We believe that this improved receptor binding and functional selectivity provides good pharmacological specificity and may result in fewer cardiovascular side effects than are commonly observed with other ß$_2$ -adrenergic receptor agonists used to treat this condition. We have developed and studied an intravenous formulation of MN-221 appropriate for hospital use.

Acute Exacerbations of Asthma:

An acute exacerbation of asthma is an acute asthma symptom episode such as shortness of breath, wheezing and chest tightness due to constricted airways. Severe acute exacerbation of asthma is an emergency situation that can lead to emergency department treatment and, in some cases, hospital admission or, more rarely, death. Inhaled short acting beta-agonist agents are the mainstays of acute treatment for these types of asthma attacks and are included in the recommended standard of care according to the National Asthma Education and Prevention Program guidelines from the U.S. Department of Health and Human Services, or DHSS, for patients suffering from acute exacerbations of asthma.

Data from the National Center for Health Statistics show that in the U.S., annual visits to emergency departments for asthma are approximately 1.75 million, and there were approximately 456,000 hospitalizations and approximately 3,447 deaths due to asthma in 2007. According to the National Heart, Lung and Blood Institute, the direct costs associated with hospital care due to asthma were estimated at $5.5 billion in the U.S. in 2010. Despite significant improvement in the long-term control treatment for asthma, we believe that the number of patients presenting to emergency departments with asthma exacerbations who do not respond to initial standard of care for asthma exacerbations and who may be admitted to the hospital for further care are very similar to these prior figures. Accordingly, we believe that there remains an unmet medical need for a safe and effective treatment for acute exacerbations of asthma that could prevent some of these hospitalizations.

In March 2012 we completed enrollment of a randomized, double-blind, placebo-controlled Phase 2 clinical trial designed to evaluate the safety and efficacy of MN-221 in patients with acute exacerbations of asthma treated in the emergency room, which involved 176 patients. The trial

was designed to compare standardized care

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to standardized care plus MN-221 at a dose of 1,200 micrograms administered intravenously over one hour. Once a patient received the initial standardized care treatment regimen, the patient was assessed for response to that treatment. If the patient s FEV1 (Forced Expiratory Volume in One Second) was less than or equal to 50 percent of predicted and the patient met all other study entry criteria, the patient was randomized to receive either MN-221 or placebo. MN-221 did not statistically meet the primary endpoint in the trial, which was improvement in FEV1 (compared to placebo). MN-221, however, showed a significant benefit over placebo for FEV1 (liters), Area Under the Curve (AUC Hour 0-1, 0-2, 0-3) of change from baseline (p=0.043, p=0.050, p=0.066 respectively). The trial also demonstrated a reduction in hospital admissions with MN-221 added to standard drug treatments. There was also significant improvement in clinical symptoms with MN-221 treated patients and the safety profile of MN-221 continues to be positive as no safety/tolerability issues of clinical significance were observed. Patients enrolled in the clinical trial continued to receive standardized care as needed. 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 future MN-221 development will be designed based on the feedback received from the FDA. In the area of COPD exacerbations, we have completed two Phase 1b clinical trials. We have determined that any future MN-221 clinical trial development will be partner-dependent from a funding perspective.

We completed a randomized, double-blind, placebo-controlled, dose escalation, multi-center Phase 2 clinical trial of MN-221 in 23 stable mild-to-moderate asthmatics in August 2007. At each dose level in the escalation, patients were randomized to receive either a 15-minute intravenous infusion of MN-221 or placebo. This clinical trial achieved statistical significance in its primary endpoint of mean change in FEV1 from baseline to measurement at 15 minutes (the end of the infusion) at doses of 10, 16, 30 and 60 micrograms per minute of MN-221 (p-value less than or equal to 0.0006) compared to placebo. MN-221 produced a significant linear, dose-related increase in mean change in post-infusion FEV1 from baseline (p-value less than or equal to 0.0001) following a 15-minute intravenous infusion of MN-221. Significant improvements in mean change in post-infusion (15 minute) FEV1 from baseline were observed at doses of 10, 16, 30 and 60 micrograms per minute (p-value less than or equal to 0.0006) and at the dose of 3.5 micrograms per minute (p-value=0.0106) compared to placebo. In the protocol correct population for this clinical trial, which consisted of 21 patients, the dose-related increases in FEV1 were maintained for four hours (p-value = 0.0393) and at eight hours (p-value = 0.0424) following the 15-minute infusion of MN-221. MN-221 was well tolerated in this Phase 2 clinical trial, with only the expected $ß_2$ -adrenergic receptor pharmacology noted in some patients (*e.g.*, fall in serum potassium, elevation in plasma glucose, mild headache and mild tremors). There were no clinically significant cardiovascular, electrocardiogram, or ECG, or vital sign changes observed at any dose tested. In addition, no serious adverse effects were observed in this clinical trial.

We completed a randomized, open-label, placebo-controlled Phase 2a clinical trial to evaluate the safety and efficacy of MN-221 in patients with moderate to severe, but stable asthma, which involved 17 patients in two dose cohorts, in September 2008. In one dosing cohort, each patient received MN-221 at a dose of 1,125 micrograms or placebo over one hour by a continuous intravenous infusion. In the other dosing cohort, each patient received MN-221 at a dose of 1,080 micrograms or placebo over two hours by a continuous intravenous infusion. Both infusion rates of MN-221 produced a marked and clinically significant improvement in FEV1. FEV1 results were expressed as percent predicted based on standard reference equations accounting for an individual s race, gender, age and height. At the end of the one-hour infusion, FEV1 increased by 17.5 percent predicted for MN-221 compared to an increase of three percent predicted for placebo. At the end of the two-hour infusion, FEV1 increased by an average of 12.1 percent predicted for MN-221 compared to an increase of 1.4 percent predicted for placebo. In accordance with the study protocol, no inferential statistical testing was performed. MN-221 was well tolerated by the patients who received either infusion rate of MN-221. There were no clinically significant safety concerns noted among adverse events, ECG data, vital sign data or laboratory assessments collected throughout this clinical trial.

We completed a randomized, modified single-blind, placebo-controlled, dose escalation Phase 2 clinical trial to evaluate MN-221 in patients with severe, acute exacerbations of asthma in emergency departments, which

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included 29 patients (13 treated with standard care only and 16 treated with MN-221 plus standard care) at planned escalating doses of 240 to 1,080 micrograms, in April 2009. All patients received standardized care consisting of inhaled albuterol, ipratropium and oral steroid treatment. No safety concerns with adding MN-221 to standardized care were identified following review of ECG laboratory and adverse experience data. The hospitalization rate among patients treated with standardized care only was 46 percent (six of 13), which was the anticipated rate, compared to a hospitalization rate of 25 percent (four of 16) among patients receiving MN-221 plus standardized care. Improvement in FEV1 values generally appeared to be greater for patients receiving MN-221 in addition to standardized treatment. As specified in the protocol for this clinical trial, no inferential statistics (*e.g.*, p-values) were calculated for this study.

We entered into an agreement to form a joint venture company with Zhejiang Medicine Co., Ltd. and Beijing Make-Friend Medicine Technology Co., Ltd. effective September 27, 2011. The joint venture agreement provides for the joint venture company, Zhejiang Sunmy Bio-Medical Co., Ltd. (Zhejiang Sunmy), to develop and commercialize MN-221 in China. A sublicense will be required under which Zhejiang Sunmy will license MN-221 from us. We have not entered into the sublicense of MN-221 with Zhejiang Sunmy as of the date of this report. There is no assurance the sublicense will be executed and there is no assurance that Zhejiang Sunmy will be able to proceed with the development of MN-221 in China.

Chronic Obstructive Pulmonary Disease Exacerbations:

A COPD exacerbation is a sustained worsening of the patient s condition that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD. Exacerbations are associated with a significant increase in mortality, hospitalization and healthcare utilization. The number of deaths due to COPD in the U.S. has more than doubled since 1980 to more than 124,000, according to a 2011 report on COPD from the American Lung Association, which used data from the Centers for Disease Control and Prevention. In 2010, according to the American Lung Association, the direct health care costs for COPD were $29.5 billion and indirect costs were $20.4 billion in the U.S. We believe there remains an unmet medical need for a safe and effective treatment for COPD exacerbations that could relieve bronchospasm and prevent some of these hospitalizations.

In July 2009 we announced our plan to evaluate MN-221 for the treatment of COPD exacerbations. Inhaled ß2-adrenergic receptor agonists, which are the current standard of care, are often inadequate to control the symptoms of COPD exacerbations. We believe that MN-221 may offer an immediate intravenous delivery for this life-threatening condition for patients who cannot get the full benefit from treatment with inhaled ß2-adrenergic receptor agonists due to severe bronchoconstriction. In addition, we believe that MN-221 may offer the potential for fewer cardiovascular side effects than older ß2-adrenergic receptor agonists due to its greater selectivity for the ß2-adrenergic receptor. This could be very significant due to the relative older age population seen in COPD patients who tend to have more underlying heart disease. On October 13, 2011, we entered into an agreement with Kissei to expand research and development services pertaining to the use of MN-221, including MN-221 for the treatment of COPD exacerbations.

We completed a randomized, double-blind, placebo-controlled Phase 1b study involving 48 moderate-to-severe COPD patients who received a one hour intravenous infusion of MN-221 at three different escalating dose levels (300 micrograms, 600 micrograms, or 1200 micrograms) or placebo in the first quarter of 2010. In March 2010, based on preliminary findings, we announced that all doses of MN-221 produced a clinically significant improvement in FEV1 (L) as compared to the baseline and placebo. At the end of the one hour infusion, FEV1(L) increased as compared to baseline by an average of 21.5 percent (p=0.0025) for the 1200 micrograms dose, 16.2 percent (p=0.020) for the 600 micrograms dose, and 9.2 percent (p=NS) for the 300 micrograms dose compared to a decrease of 4.0 percent for the placebo. MN-221 at doses of 600 micrograms and 1200 micrograms appeared to have an effect for at least six hours as compared to placebo. MN-221 was well tolerated by all patients who received infusions of MN-221.

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In August 2012 we completed a Phase 1b/2a clinical trial of MN-221 for the treatment of moderate to severe COPD patients. A total of 25 subjects were randomized to placebo (5 subjects) or MN-221 (20 subjects) treatment groups; with similar enrollment at each of two clinical research units. The patient group included those who had concomitant illnesses and were using other medications that are typical in this disease population. In addition, we tested the safety, tolerability, pharmacokinetics, and preliminary efficacy of repeat-administration placebo or MN-221 (1,200 micrograms) over a few days of residence in a clinical trial unit, and we assessed the correlation and potential future clinical trial utility of certain respiratory function test devices. Efficacy results indicated moderately improved pulmonary function (FEV1) in the MN-221 recipients but not the placebo recipients. Moreover, the improvement of FEV1 on subsequent MN-221 dosing days was as good as or better than treatment on day one. Our comparison of the simple hand-held FEV1 monitor with the spirometer machine used in our other clinical trials of MN-221 indicated good correlation and pharmacokinetic analyses indicated no significant accumulation of plasma MN-221 over the multiple dosing intervals.

Our other product development programs consist of the following:

- MN-001 for the treatment of bronchial asthma, for which we initiated a Phase 3 clinical program in the fourth quarter of 2006 that we subsequently terminated in the second quarter of 2007, and for which we developed prototypes of once-per-day oral dosing formulations;

- MN-001 for the treatment of interstitial cystitis, for which we completed a Phase 2 clinical trial in the first quarter of 2007;

- MN-029 for the treatment of solid tumors, for which we completed one Phase 1 clinical trial in the second quarter of 2006 and one Phase 1 clinical trial in the fourth quarter of 2007;

- MN-305 for which we completed a Phase 2 clinical trial for the treatment of generalized anxiety disorder in the second quarter of 2006 and a Phase 2 clinical trial for the treatment of insomnia in the fourth quarter of 2007;

- MN-221 for the treatment of preterm labor, for which we completed a Phase 1 clinical trial to investigate the pharmacokinetic profile of MN-221 in healthy pregnant women not in labor in the second quarter of 2007;

- MN-246 for the treatment of urinary incontinence, for which we completed a Phase 1 clinical trial in the fourth quarter of 2006 and a Phase 1 food effects study in the first quarter of 2007;

- MN-447 for the treatment of thrombotic disorders, which remains in preclinical development; and

- MN-462 for the treatment of thrombotic disorders, which remains in preclinical development.

Sales and Marketing

We currently have no marketing and sales capabilities and we expect to rely on a strategic partner to complete late stage product development and commercialize our products.

Manufacturing

We rely on third parties to manufacture bulk active pharmaceutical ingredients, or 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-Teva Pharmaceuticals (Taisho). We are currently working with Taisho on further formulation development to address our future clinical trial needs.

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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 such product candidate is approved for commercial sale by the FDA or other regulatory authorities. In September 2011, we entered into a letter agreement with Kissei pursuant to which, among other provisions, we agreed upon a new price for clinical supplies of API.

In March 2009, we entered into an agreement with Hospira Worldwide, Inc., or Hospira, for the completion of pre-commercialization manufacturing development activities and the manufacture of commercial supplies of finished product for MN-221 utilizing Hospira s proprietary ADD-Vantage drug delivery system, if such product candidate is approved for commercial sale by the FDA or other regulatory authorities. Pursuant to the terms of the agreement with Hospira, Hospira will receive development fees from us upon completion of specified development activities, which we will expense as the costs are incurred. We are also obligated under the agreement to purchase a minimum number of units each year following regulatory approval, which number will be based on our forecasts submitted to Hospira on a rolling basis. In addition to the agreement with Hospira, we anticipate entering into a commercial supply agreement with a contract manufacturer for finished product of MN-221 in standard vials. However, at present, we do not have an established agreement regarding the commercial supply of MN-221 in standard vials or for the API or finished product of any of our product candidates.

Intellectual Property and License Agreements

Since our inception in September 2000, we have entered into eight license agreements with pharmaceutical companies which cover our current product candidates. We have also entered into license agreements with universities, including the University of Colorado and the University of Adelaide, 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. To date, we have obtained licensed rights under 14 issued U.S. patents. We also have obtained licensed rights to 93 issued and pending foreign patents and applications corresponding to these U.S. patents and patent applications. In addition to these licensed rights, we hold 15 issued U.S. patents and have filed 17 additional U.S. patent applications. We also hold 151 issued and pending foreign patents and 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

On October 22, 2004, we entered into an exclusive license agreement with Kyorin Pharmaceutical for the development and commercialization of MN-166. Kyorin Pharmaceutical 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 for the treatment of MS, except for ophthalmic solution formulations. MN-166 is not covered by a composition of matter patent. The U.S. method of use patent for MN-166 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 Pharmaceutical an exclusive, royalty-free, sub-licensable license to use the preclinical, clinical and regulatory databases to develop ophthalmic products incorporating the MN-166 compound anywhere in the world and non-ophthalmic products incorporating the MN-166 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 Pharmaceutical or, in the event that a third party claims that MN-166 infringes upon such third party s intellectual property rights, with 30 days written notice.

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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 Pharmaceutical 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 Pharmaceutical $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 ten pending U.S. patent applications as well as corresponding pending foreign patent applications covering MN-166 (ibudilast) and its analogs. These patents and patent applications are primarily related to our development portfolio of small molecule-based products and are currently directed to methods of treating various indications using 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. The patent, which was granted in March 2012, will expire no earlier than November 2029, which does not include a potential extension under patent term restoration rules, and covers a method of treating primary progressive multiple sclerosis (PPMS) or secondary progressive MS (SPMS) by administering ibudilast either alone or in combination with other drugs. 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 U.S. and it expires no earlier than December 2025. 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 drug addiction or drug dependence or withdrawal syndrome in the U.S. and it expires no earlier than January 2030. We received a Notice of Allowance for a pending patent application, based on this U.S. patent in drug addiction, from the European Patent Office (EPO) and a patent maturing from this application is expected to expire no earlier than September 2026. We received a Notice of Allowance for a pending patent application that covers the use of MN-166 (ibudilast) to enhance opioid analgesia in acute pain settings from the European Patent Office (EPO) and a patent maturing from this application is expected to expire no earlier than January 2028. A similar patent application to this allowed European patent is pending in the U.S.

MN-221

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 First Section of 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 and patent applications in foreign countries and is sub-licensable upon receipt of the written consent of Kissei. The U.S. patent for MN-221 has composition of matter and method of use claims. The U.S. composition of matter patent underlying the license issued on October 17, 2000 and is set to expire no earlier than February 18, 2017. Corresponding composition of matter patents in various other countries are set to expire no earlier than February 18, 2017.

In addition to the licensed patents, we have filed patent applications in the U.S. and certain foreign countries regarding additional uses and formulations of MN-221. We have received a Notice of Allowance from the U.S. Patent and Trademark Office for a pending patent application, which covers the use of MN-221 for the treatment of acute exacerbations of asthma. The MN-221 patent maturing from this allowed patent application is expected to expire no earlier than November 2030 and includes claims covering the use of MN-221 (bedoradrine) in

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combination with a standard of care (SOC) treatment regimen. The allowed claims include specific coverage for different routes of administration, including intravenous, oral and inhalation. Counterparts of this patent application are pending in certain foreign jurisdictions.

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 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 the letter agreement we entered into with Kissei in September 2011, we agree to renegotiate in good faith with Kissei the existing levels of the milestone payment amounts and royalty rates.

MN-001

On March 14, 2002, we entered into an exclusive license agreement with Kyorin Pharmaceutical for the development and commercialization of MN-001. 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 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. patent and certain corresponding patents in foreign countries. The U.S. composition of matter patent for MN-001 underlying the license expired on February 23, 2009, and the U.S. composition of matter patent for MN-002 underlying the license expired on December 30, 2011. Foreign composition of matter patents for MN-001 and MN-002 have also expired. We intend to rely upon the applicable period of post-approval exclusivity, in addition to any patents that may issue from our own patent applications. Under the terms of the agreement, we granted to Kyorin Pharmaceutical an exclusive, royalty-free, sub-licensable license to use the preclinical, clinical and regulatory databases to develop ophthalmic products incorporating the MN-001 compound anywhere in the world and non-ophthalmic products incorporating the MN-001 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, and we may terminate the agreement for any reason with 90 days written notice to Kyorin Pharmaceutical 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 Pharmaceutical 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 Pharmaceutical $4.0 million 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.

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We filed and the U.S. Patent and Trademark Office issued eight U.S. patents covering certain compositions, uses and manufacturing processes associated with MN-001 and its metabolite, MN-002. Patent applications corresponding to these U.S. patents were filed in certain foreign countries and some of the foreign patents have issued.

MN-029

On June 19, 2002, we entered into an exclusive license agreement with Angiogene Pharmaceuticals for the development and commercialization of the ANG-600 series of compounds. Angiogene Pharmaceuticals 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. This license includes an exclusive, sub-licensable license under -four U.S. patents and certain corresponding patents and patent applications in foreign countries. The U.S. composition of matter patent for MN-029, which issued on November 11, 2003, is set to expire on January 14, 2020. Patent applications corresponding to this U.S. patent were filed in certain foreign countries and some of those foreign patents have been issued. The U.S. patent covering methods of treating solid cancer tumors by administering MN-029, which issued on July 25, 2006, is set to expire in July, 2020.

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 Pharmaceuticals.

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 Pharmaceuticals 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 Pharmaceuticals $1.4 million to date and are obligated to make payments of up to $16.5 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.

MN-305

On April 27, 2004, we entered into an exclusive license agreement with Mitsubishi Pharma Corporation, the predecessor to Mitsubishi Tanabe Pharma Corporation, for the development and commercialization of MN-305. Mitsubishi Tanabe Pharma Corporation 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, Singapore, Brunei, Thailand, Malaysia, Indonesia, the Philippines, Vietnam, Bangladesh, Pakistan, South Korea, China and Taiwan), sub-licensable license to the patent rights and know-how related to MN-305 and its active metabolite disclosed and included or covered by these patents for all indications. The license is sub-licensable upon receipt of the written consent of Mitsubishi Tanabe Pharma Corporation. This license includes an exclusive, sub-licensable license under five U.S. patents and certain corresponding patents and patent applications in foreign countries. The U.S. composition of matter patent for MN-305, which issued on December 1, 1992, expired on March 14, 2011. Patent applications corresponding to this U.S. patent were filed in certain foreign countries, and these foreign counterparts expired on or before March 14, 2011. The U.S. patent covering the use of MN-305 to treat anxiety, which issued on August 10, 1993, expired on March 14, 2011.

Under the terms of the agreement, we granted to Mitsubishi Tanabe Pharma Corporation a license to use our know-how and patents relating to MN-305 to develop products incorporating the MN-305 compound outside of our territory. Mitsubishi Tanabe Pharma Corporation also has the right to co-promote licensed products in our territory on terms to be agreed upon by the parties.

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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 if, in our reasonable opinion, the safety, patient tolerability, efficacy, profile or commercial viability of MN-305 does not justify continued development with 90 days written notice to Mitsubishi Tanabe Pharma Corporation or, in the event that a third party claims that the licensed intellectual property related to MN-305 infringes 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 ten years from the date of first commercial sale in a specific country or the expiration of a valid patent claim in such country. In the event that we enter into a sublicense with a third party, the term of the agreement will extend for as long as we receive royalty payments from such third party.

Under the license agreement, we have paid Mitsubishi Tanabe Pharma Corporation $1.0 million to date, and we are obligated to make payments of up to $18.8 million based on the achievement of certain clinical, regulatory and sales milestones. We are also obligated to pay a royalty on net sales of the licensed products.

MN-246

On December 8, 2004, we entered into an exclusive license agreement with Mitsubishi Pharma Corporation, the predecessor to Mitsubishi Tanabe Pharma Corporation, for the development and commercialization of MN-246. We obtained an exclusive, worldwide (excluding Japan, Singapore, Brunei, Thailand, Malaysia, Indonesia, the Philippines, Vietnam, Bangladesh, Pakistan, South Korea, China and Taiwan), sub-licensable license to the intellectual property surrounding MN-246, its derivatives and any other compounds disclosed or claimed in the licensed Mitsubishi Tanabe Pharma Corporation patent assets. The license is sub-licensable upon receipt of the written consent of Mitsubishi Tanabe Pharma Corporation and includes an exclusive license under one U.S. patent and certain corresponding patents in foreign countries. The U.S. patent covering MN-246 and methods of making and using MN-246, which issued on May 30, 2000, is set to expire on October 24, 2016. Patent applications corresponding to this U.S. patent were filed in certain foreign countries, and these foreign counterparts are set to expire no earlier than October 24, 2016.

The issued U.S. patent covers generic phenylethanolamines encompassed by a given chemical formula, inc