MEDICINOVA INC
Form 10-K
March 29, 2012
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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, 2011

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 or Organization)	**(I.R.S. Employer Identification No.)**
4350 La Jolla Village Drive, Suite 950, San Diego, CA	**92122**
(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 $41,116,072 based on the closing price of the registrant s common stock on the Nasdaq Global Market of $2.69 per share on June 30, 2011. 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, 2012 was 16,088,015.

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 2012 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. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant s fiscal year ended December 31, 2011.

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MEDICINOVA, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2011

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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; our ability to integrate Avigen s ibudilast development program with ours; 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 acquiring and developing novel, small molecule therapeutics for the treatment of serious diseases with unmet medical needs with a specific focus on the U.S. market. Through strategic alliances, primarily with Japanese pharmaceutical companies, we hold rights to a diversified portfolio of clinical and preclinical product candidates which we believe provide significant commercial opportunity for the Company. In December 2009 we acquired Avigen Inc., or Avigen, a biopharmaceutical company that focused on identifying and developing differentiated products to treat patients with serious disorders, whose potential product candidate is a macrophage migration inhibitory and a glial attenuator for central nervous system, or CNS, disorders such as neuropathic pain, opioid addiction and withdrawal and methamphetamine addiction.

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We believe that our ability to gain access to and acquire potentially high-value product candidates from Japanese and European pharmaceutical companies is largely attributable to the established relationships and broad industry experience of our management team. In particular, we believe our relationships with Japanese pharmaceutical companies and their executives provide us with a competitive advantage in opportunistically sourcing product candidates from Japanese pharmaceutical companies at attractive terms. Since our inception, we have established relationships with a number of pharmaceutical companies, including Kissei Pharmaceutical Co., Ltd., or Kissei Pharmaceutical, Kyorin Pharmaceutical Co., Ltd., or Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma Corporation and Meiji Seika Kaisha, Ltd., or Meiji Seika Kaisha, in Japan and Angiogene Pharmaceuticals, Ltd., or Angiogene Pharmaceuticals, in the United Kingdom, pursuant to which we have obtained rights to develop and commercialize our current product candidates.

Since our inception, 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, multiple sclerosis (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. Two of such compounds have been in preclinical development for the treatment of thrombotic disorders. In addition, we have expanded our development program for MN-221 for the treatment of chronic obstructive pulmonary disease (COPD) exacerbations.

At present, we are focusing our resources on the following prioritized product development programs:

Product Candidate	Disease/Indication	Phase of Development	Licensor	Licensed Territory
MN-221	Acute exacerbations of asthma and COPD exacerbations	Phase 2 clinical trial in emergency rooms at planned escalating doses in patients with severe, acute exacerbations of asthma completed in the second quarter of 2009	Kissei Pharmaceutical	Worldwide, except Japan*
		Phase 2 clinical trial (CL-007) in emergency rooms to evaluate safety and efficacy in patients with acute exacerbations of asthma initiated in the first quarter of 2009. On March 21, 2012 we announced completion of the 176 patient enrollment of the Phase 2 MN-221-CL-007 clinical trial. We expect trial results in the second quarter of 2012.		
		Phase 1b clinical trial to evaluate the safety and efficacy in patients with stable, moderate to severe COPD completed in the first quarter of 2010.		

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Product Candidate	Disease/Indication	Phase of Development	Licensor	Licensed Territory
		Encouraging safety and efficacy data for the -007 trial was reported via press release in the first quarter of 2010 and at the CHEST Society meeting later in 2010. In the first quarter of 2012 we initiated an additional Phase 1b COPD clinical trial that has commenced enrollment and has an anticipated trial completion around the end of the second quarter of 2012.		
MN-166	CNS disorders**	Phase 2 clinical trial completed in the second quarter of 2008.	Kyorin Pharmaceutical (MN-166)	Worldwide, except Japan, China, Taiwan and South Korea (MN-166)
		Prototype once-per-day oral formulation developed for future clinical trials		
		Phase 1b/2a clinical trial in diabetic neuropathic pain completed in the fourth quarter of 2007		
		Phase 1b National Institute on Drug Abuse, or NIDA, funded clinical trial in methamphetamine-dependent volunteers initiated in the fourth quarter of 2010		
		Phase 1b/2a NIDA funded clinical trial to evaluate safety and efficacy in heroin-dependent volunteers completed in the fourth quarter of 2010		
		Investigator initiated Phase 2 clinical trial collaboration with a headache and pain specialist in Australia initiated in the third quarter of 2011		

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* Pursuant to our license agreement with Kissei Pharmaceutical, Kissei has the right to co-promote licensed products in our territory on terms to be agreed upon by the parties. 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 to develop and commercialize MN-221 in China. A sublicense under which the joint venture company will license MN-221 from us will be required, which sublicense will require the consent of Kissei. We have not entered into the sublicense of MN-221 with the joint venture company as of the date of this report. There is no assurance the sublicense will be executed and there is no assurance that the joint venture company will be able to proceed with the development of MN-221 in China.

** Other CNS disorders encompass MS, neuropathic pain, opioid addiction and withdrawal and methamphetamine addiction.

Upon completion of proof-of-concept Phase 2 clinical trials, we intend to enter into strategic alliances with leading pharmaceutical or biotech companies to support further clinical development if we are unable to raise additional capital to conduct Phase 3 trials. Depending on the results of our the MN-221 Phase 2 trial that completed enrollment in March 2012 and our ability to raise additional capital and/or to enter into a collaboration with a leading pharmaceutical or biotech company, we intend to define a Phase 3 trial and other development plans for MN-221 for the treatment of acute exacerbations of asthma and conduct one or more Phase 3 trials, and we intend to pursue the development of this drug candidate for the treatment of COPD. We also intend to enter into strategic alliances with leading pharmaceutical or biotech companies to support further clinical development of MN-166. We may also pursue potential partners and potential acquirers of license rights to our programs in markets outside the U.S. In addition, we continue to limit development activities for the balance of our existing product development programs in order to focus on our prioritized product development programs. For each of these remaining product candidates, we plan to conduct development activities only to the extent deemed necessary to maintain our license rights or maximize their value while pursuing a variety of initiatives to monetize such development programs. We cannot assure you that we will be successful in monetizing these programs on attractive terms, or at all. See *Risk Factors.*

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Our eight non-prioritized product development programs consist of the following:

Product Candidate	Disease/Indication	Phase of Development	Licensor	Licensed Territory
MN-001*	Bronchial asthma	Phase 3 clinical trial initiated in the fourth quarter of 2006 and terminated in the second quarter of 2007; Once-per-day oral dosing formulation prototypes developed	Kyorin Pharmaceutical	Worldwide, except Japan, China, Taiwan and South Korea
MN-001	Interstitial cystitis	Phase 2 clinical trial completed in the first quarter of 2007	Kyorin Pharmaceutical	Worldwide, except Japan, China, Taiwan and South Korea
MN-029	Solid tumors	Phase 1 clinical trial completed in the second quarter of 2006; Second Phase 1 clinical trial completed in the fourth quarter of 2007	Angiogene Pharmaceuticals	Worldwide
MN-305	Generalized anxiety disorder/ Insomnia	Phase 2 clinical trial completed in generalized anxiety disorder in the second quarter of 2006 ; Phase 2 clinical trial in insomnia completed in the fourth quarter of 2007	Mitsubishi Tanabe Pharma Corporation	Worldwide, except Japan and certain other countries in Asia
MN-221	Preterm labor	Phase 1 clinical trial completed in the second quarter of 2007	Kissei Pharmaceutical	Worldwide, except Japan
MN-246	Urinary incontinence	Phase 1 clinical trial completed in the fourth quarter of 2006; Phase 1 food effects study completed in the first quarter of 2007	Mitsubishi Tanabe Pharma Corporation	Worldwide, except Japan and certain other countries in Asia
MN-447	Thrombotic disorders	Preclinical	Meiji Seika Kaisha	Worldwide, except Japan and certain other countries in Asia
MN-462	Thrombotic disorders	Preclinical	Meiji Seika Kaisha	Worldwide, except Japan and certain other countries in Asia

* Our rights to MN-001 licensed from Kyorin Pharmaceutical exclude ophthalmic solution formulations.
Although positive signs of efficacy were obtained in the clinical trials conducted on MN-001 in interstitial cystitis and MN-305 in generalized anxiety disorder, the predefined primary statistical endpoints of the clinical trials were not achieved; therefore, we would not anticipate submitting either clinical trial as a pivotal trial supporting a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or the FDA.
In the Phase 2 clinical trial conducted on MN-305 in insomnia, the predefined statistical endpoint of the clinical trial was not achieved; therefore, we terminated any further development of MN-305 for the treatment of insomnia.

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Our Strategy

Our goal is to build a sustainable biopharmaceutical business through the successful acquisition, development and commercialization 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:

Concentrate our resources on our two prioritized product development programs, MN-221 and MN-166. Depending on the results of our the MN-221 Phase 2 trial that completed enrollment in March 2012 and our ability to raise additional capital and/or to enter into a collaboration with a leading pharmaceutical or biotech company to fund development costs, we intend to define a Phase 3 trial and other development plans for MN-221 for the treatment of acute exacerbations of asthma and conduct one or more Phase 3 trials, and we intend to pursue the development of this drug candidate for the treatment of COPD. We also intend to enter into strategic alliances with leading pharmaceutical or biotech companies to support further clinical development of MN-166. We may also decide to pursue potential partners and potential acquirers of license rights to our programs in markets outside the U.S.

Pursue additional indications and commercial opportunities for our prioritized product candidates. We will seek to maximize the value of MN-221 and MN-166 by pursuing other potential indications and commercial opportunities for such product candidates. For example, we have rights to develop and commercialize MN-221 for any disease or indication. In addition to the ongoing evaluation of MN-221 for the treatment of acute exacerbations of asthma, we expanded our development program for MN-221 to evaluate MN-221 for the treatment of COPD exacerbations utilizing our existing Investigational New Drug Application, or IND for MN-221.

Maximize the value of the remainder of our diversified pipeline of existing product candidates. We will conduct development activities strategically on the remainder of our existing product candidates, to the extent that we deem any further activities necessary to maintain our license rights or maximize their value, while aggressively pursuing a variety of initiatives to monetize these product candidates on appropriate terms.

Opportunistically in-license additional product candidates through our global industry relationships. Over the long term, we intend to expand our pipeline of in-licensed product candidates by continuing to cultivate and strengthen our business relationships with pharmaceutical companies in Japan and other markets. We believe our ability leverage industry relationships to acquire product candidates with high potential and existing preclinical or early clinical data from Japanese pharmaceutical companies provides us with a competitive advantage over other drug development companies in the U.S. market. We believe that additional diversification and expansion of our pipeline of product candidates will help maximize the commercial opportunity and mitigate the risks inherent in drug discovery and development.

Strategically partner with pharmaceutical companies who are leaders in their fields to complete late stage product development and successfully commercialize our products. We develop and maintain business development relationships with pharmaceutical therapeutic area leaders who seek late stage product candidates to complete development and commercialization. We intend to select partners with demonstrated ability to complete late stage development and successfully commercialize product candidates. To ensure our ability to build a sustainable business, we may selectively add commercial capabilities to our management team to support our evolution into a commercial entity as our product development programs mature.

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 our product candidates offer innovative therapeutic approaches that may provide significant advantages relative to current therapies.

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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 details of our product development programs:

Prioritized Product Candidates

The current state of the development program for each of our two prioritized product candidates is described below.

MN-221 for Acute Exacerbations of Asthma

Indication Overview and Market Opportunity. 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 exacerbations 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 Guideline Clearinghouse 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 was 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 which may be admitted to the hospital for further care are very similar to these prior figures. Hence 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.

Overview of MN-221 in Acute Exacerbations of Asthma. 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 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.

Clinical Results of MN-221 in Acute Exacerbations of Asthma. 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

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primary endpoint of mean change in forced expiratory volume in one second, or FEV_1, 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 FEV_1 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) FEV_1 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 FEV_1 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 FEV_1. FEV_1 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, FEV_1 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, FEV_1 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 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 FEV_1 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.

Development Plan of MN-221 in Acute Exacerbations of Asthma. 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 severe, acute exacerbations of asthma in emergency departments, which involved 176 patients. The trial was designed to compare standardized care to standardized care plus MN-221 at a dose of 1,200 micrograms administered intravenously over one hour. Once a patient has received the initial standardized care treatment regimen, the patient will be assessed for response to that treatment. If the patient s FEV_1 is less than or equal to 50 percent of predicted and the patient meets all other study entry criteria, the patient will be randomized to receive either MN-221 or placebo. Patients enrolled in the clinical trial will continue to receive standardized care as needed. The primary efficacy endpoint will be improvement in FEV_1. We expect trial results in the second quarter of 2012. Should we have acceptable findings, we intend to define a

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Phase 3 trial and other development plans and request an End-of-Phase 2 meeting with the FDA. Depending on the results of our the MN-221 Phase 2 trial and our ability to raise additional capital and/or to enter into a collaboration with a leading pharmaceutical or biotech company, we intend to initiate our Phase 3 program.

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 to develop and commercialize MN-221 in China. A sublicense under which the joint venture company will license MN-221 from us will be required, which sublicense will require the consent of Kissei. We have not entered into the sublicense of MN-221 with the joint venture company as of the date of this report. There is no assurance the sublicense will be executed and there is no assurance that the joint venture company will be able to proceed with the development of MN-221 in China.

MN-221 for Chronic Obstructive Pulmonary Disease Exacerbations

Indication Overview and Market Opportunity. A COPD exacerbation is a sustained worsening of the patient s condition, from the stable state and beyond normal day-to-day variations, 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. According to data from the National Heart, Lung, and Blood Institute, an estimated 12.1 million adults had a diagnosis of COPD in the U.S. in the year 2001 and about 24 million adults have evidence of impaired lung function indicating that COPD is under diagnosed. According to data from the National Heart, Lung, and Blood Institute, in the year 2000, there were 119,000 deaths, 726,000 hospitalizations, and 1.5 million hospital emergency department visits due to COPD in the U.S. The age-adjusted death rate for COPD increased more than 30 percent since 1980, according to a 2010 report on COPD from the American Lung Association, which used data from the Centers for Disease Control and Prevention. In 2002, according to the National Heart, Lung, and Blood Institute, direct costs for COPD were $18.0 billion and indirect costs were $14.1 billion in the U.S. In 2010, according to the American Lung Association, the direct costs for COPD were approximately $29.5 billion and indirect costs were approximately $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.

Overview of MN-221 in COPD Exacerbations. 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. The current CL-012 trial, wherein enrollment is expected to be completed around the end of the second quarter of 2012, is a component of that agreement.

Clinical Results of MN-221 in 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 FEV_1 (L) as compared to the baseline and placebo. At the end of the one hour infusion, FEV_1 (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

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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.

Development Plans of MN-221 in COPD Exacerbations. In the first quarter of 2012 we initiated a Phase 1b/2a clinical trial in severe to moderate COPD patients which addresses a number of important goals in developing MN-221 in this indication. The trial design includes enrollment of approximately 20 patients with co-morbidities and concomitant medications that typify patients that might present in Emergency Departments s with exacerbations. In addition, we will be exploring the safety, tolerability, pharmacokinetics, and preliminary efficacy of repeat-administration placebo or MN-221 (1.2 mg) over a few days of residence in a clinical trial unit. Finally, we are assessing the correlation and potential future clinical trial utility of certain breathing function testing devices. The protocol has received FDA and IRB review and we anticipate completing this trial by the end of the second quarter of 2012.

Ibudilast (MN-166)

The Ibudilast portfolio, which includes the Phase 2-staged lead drug compound and proprietary analogs, represents novel, first-in-class, non-opioid drugs for the treatment of several large pain and drug addiction indications. Ibudilast 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, a 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 that may contribute to its attenuation of neuroinflammation. While considered a New Molecular Entity, or NME, in the U.S. and Europe, it involves redirection of an approved drug, ibudilast, which was first approved in Japan more than 20 years ago. Ibudilast has been prescribed to over one million patients for a different indication and has a good post-marketing safety profile as reported in nearly 15,000 patients studied at the prescribed doses.

Based on our research, we have filed for patents protecting multiple uses of ibudilast in neurological conditions, as well as for 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. As NMEs, MN-166 and its analogs would be entitled to five years of marketing exclusivity from first approval in the U.S. and up to 10 years of exclusivity in the European Union

Neuropathic pain: MIF activity and glial activation in the brain and spinal cord contribute to the establishment and amplification of the chronic pain state. As part of Avigen s program investigating glial attenuation as a novel approach to the treatment of neuropathic pain, Avigen conceived and demonstrated that ibudilast was efficacious in preclinical models of neuropathic pain and may be effective in a wide range of neuropathic pain syndromes including neuropathy, 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 completed Avigen preclinical and clinical development. A Phase 2 investigator-sponsored trial of ibudilast in the treatment of chronic medication overuse headache (MOH) pain is also ongoing in Australia and involves placebo or ibudilast administration for up to two months.

Opioid withdrawal: A Phase 1b/2a clinical trial in opioid withdrawal and analgesia, or OWA, was completed and funded by NIDA and conducted at Columbia University by leading specialists in the study and

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treatment of substance abuse. MN-166 and analogs have been shown in preclinical models of opioid (morphine or oxycodone) withdrawal to significantly reduce withdrawal symptoms. Moreover, MN-166 attenuates both behavioral and neurochemical markers of opioid reward. 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 ($p<0.05$ for 80 mg/d treatment arm relative to placebo control on the Subjective Opioid Withdrawal Scale (SOWS) endpoint) and enhanced opioid analgesia ($p<0.05$ for the McGill Pain Questionnaire endpoint for the 80 mg/d treatment arm vs. placebo control). Other measures of withdrawal (Clinicians Opioid Withdrawal Scale) or analgesia (quantitative time endpoints for cold pressor test) were not significantly attenuated.

Methamphetamine addiction: In collaborative studies with NIDA, MN-166 has demonstrated utility in methamphetamine relapse in animals which translated into a NIDA-funded exploratory Phase 1b methamphetamine interaction clinical trial with investigators at the University of California Los Angeles. The trial is currently enrolling patients.

Development Plans of Ibudilast for Neuropathic Pain and Drug Addiction. We are not planning to undertake Phase 2b clinical development of ibudilast for pain or drug addiction indications until such time as we are successful in entering into a strategic collaboration and/or funding arrangement to support further clinical development of our combined MN-166 ibudilast-based programs. We are actively pursuing potential partners for such purpose.

Ibudilast (MN-166) for Progressive Multiple Sclerosis

Indication Overview and Market Opportunity. 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. In addition, according to the National Multiple Sclerosis Society, approximately 200 people are diagnosed with MS in the U.S. each week. 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. Approximately 50% 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 the most recent annual reports of leading MS drug companies, including Biogen Idec Inc., Merck Serono S.A., Teva Pharmaceuticals Industries Ltd. And Bayer Shering Pharma AG, worldwide sales of drugs to treat MS exceeded $11 billion in 2010.

The aim of treatment is to relieve symptoms of acute attacks by reducing the frequency of relapses and limiting the disabling effects of relapses and to minimize disability caused by disease progression. Steroids are used in treating MS to decrease the severity and shorten the duration of the attacks, but they do not change the course of the disease. Corticosteroid use is normally limited to the short-term treatment of MS, perhaps over a period of one to three weeks, as it generally is believed that the side effects and safety risks of long-term corticosteroid therapy outweigh clinical benefits in extended MS treatment. More recently, immunosuppressive agents and techniques have been introduced for the treatment of MS. However, these treatments are only partially effective and certain side effects may preclude their widespread use. These treatments may slow the course of disease progression and mitigate its effects temporarily, but additional drugs are often required to address the various CNS dysfunctions caused by the disease. Progressive MS (PPMS and SPMS) represents a particularly unmet pharmacotherapy need as there are little or no clearly effective, safe, and well-tolerated drugs approved.

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Overview of MN-166 for Progressive Multiple Sclerosis. We licensed MN-166 from Kyorin Pharmaceutical in October 2004. MN-166 has been marketed in Japan and Korea since 1989 to treat cerebrovascular disorders and bronchial asthma. In preclinical *in vivo* and *in vitro* studies, MN-166 inhibited leukotriene activity, phosphodiesterases and nitric oxide synthase, all of which are inflammatory mechanisms known to be involved in MS. These studies also suggested that MN-166 may suppress the production of pro-inflammatory cytokines (IL-1ß, TNF-a and enhance the production of the anti-inflammatory cytokines (IL-4, IL-10). Based on the potential mechanisms of action of MN-166, its clinical safety history in Japan, the results of pilot studies conducted by Kyorin Pharmaceutical in MS patients and the issuance of a U.S. patent covering the method of using MN-166 to treat the disease, we decided to pursue development of MN-166 as a novel, oral agent for the treatment of MS.

Clinical Results of MN-166 for Progressive Multiple Sclerosis. 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 one open-label pilot clinical trial, the investigators studied the effects of MN-166 on relapse rates in six MS patients who had a mean of four relapses per year. Following 12 to 20 months of treatment with MN-166, the average relapse rate was reduced. Over this time frame, there was no significant change in the mean Expanded Disability Status Score, or EDSS, a measure of MS drug efficacy and disease progression. No side effects of MN-166 were reported in this clinical trial. In a second pilot trial involving 12 MS patients receiving MN-166 for four weeks, 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.

Development Plans of MN-166 for Progressive Multiple Sclerosis. Based on some of our prior Phase 2 RRMS trial outcomes and opinions provided by multiple sclerosis experts and advisors, MN-166 may be best positioned as a therapy for progressive MS. Combined with the recent USPTO allowance of our method of use

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patent providing exclusivity for ibudilast in treating progressive MS, including SPMS, we are formulating development plans. It is our intent to advance MN-166 into a Phase 2 proof-of-concept trial in progressive MS and to fund that development via strategic collaboration with a corporate partner and/or funding agency(ies). There can be no assurance that we will be able to successfully secure such strategic collaborations or fundraising activities.

MN-001 for Asthma

Indication Overview and Market Opportunity. Asthma is a chronic inflammatory disease of the airways in which symptom control is the key to effective disease management. Alleviation of acute asthmatic symptoms and blocking of late phase inflammation are both important to asthma therapy. According to the CDC and the Global Initiative for Asthma, there are approximately 24.6 million asthma patients in the U.S. and over 300 million asthma patients worldwide.

Overview of MN-001 in Asthma. MN-001 is a novel, orally bioavailable compound being developed for the treatment of bronchial asthma. We licensed MN-001 from Kyorin Pharmaceutical in March 2002. In *in vivo* preclinical studies conducted by Kyorin Pharmaceutical and us, MN-001 combined the positive attributes of the leukotriene antagonists and inhaled steroids, while maintaining an acceptable safety profile.

In preclinical pharmacology studies, MN-001 inhibited airway hyper-reactivity through a reduction of airway inflammation. *In vitro* studies and animal studies also suggested that MN-001 may affect many of the downstream mechanisms activated by mast cell degranulation, which is the release of chemicals that cause inflammation. MN-001 also demonstrated that it is a potent inhibitor of pro-inflammatory enzymes *in vitro* (*e.g.*, 5-lipoxygenase and phosphodiesterase 4), as it prevented migration of inflammatory cells to the lungs of rodents in these studies. In addition, in guinea pig asthma models, MN-001 was more selective than steroids in affecting cells involved in the inflammatory process and not those involved in cellular immunity.

Clinical Results of MN-001 for Asthma. MN-001 has proven to be well tolerated in early clinical testing. Treatment-related adverse effects, primarily consisting of gastrointestinal discomfort such as diarrhea, loose stools, nausea and upper abdominal pain, were mild, transient and reversible. These adverse effects were consistent with findings in preclinical studies.

We conducted a randomized, double-blind, placebo-controlled, multi-center Phase 2 clinical trial in patients with mild-to-moderate asthma, which was completed in the fourth quarter of 2005. In this clinical trial, 147 patients were randomly assigned to receive placebo or MN-001 tablets in one of three oral dosing regimens for four weeks. The primary endpoint of the trial was achieved with a statistically significant improvement in FEV_1 after four weeks of treatment with 500 mg of MN-001 at three times daily dosage, or TID, compared to placebo (p-value=0.021; intent-to-treat, observed cases). A similar trend was observed for the 750 mg two times daily dosage, or BID, of MN-001 (p-value=0.058). Positive trends in secondary outcome measures were also observed in the 500 mg TID treatment group, including serial spirometry, morning and evening peak flow rates, and provocative concentration causing a 20 percent fall in FEV_1, or PC20, values in a methacholine challenge test, each of which is a common measure of respiratory function. MN-001 was well tolerated in this clinical trial with 89 percent of patients completing four weeks of treatment. There was no apparent difference between placebo and any of the active treatment groups in adverse events leading to discontinuation or in adverse events attributable to treatment.

MN-001 for Interstitial Cystitis

Indication Overview and Market Opportunity. Interstitial Cystitis (IC) is a chronic disease of the bladder characterized by urinary frequency and urgency, nighttime urination and pelvic and bladder pain. It is widely believed that IC is due to an altered or defective bladder lining and an increased number of activated bladder mast cells, which are specialized cells that release biochemicals and cause inflammation. According to the

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National Kidney and Urologic Diseases Information Clearinghouse, which is a division of the National Institutes of Health, at least 1.3 million patients suffer from IC in the U.S., and more than one million of them are women. We believe that IC is currently under diagnosed and that the market for drugs that treat IC will likely expand with the introduction of effective new treatments.

Overview of MN-001 for Interstitial Cystitis. MN-001 is a novel, orally bioavailable, anti-inflammatory compound being developed for the treatment of IC. Data that we collected in connection with the development of MN-001 for bronchial asthma and data collected by Kyorin Pharmaceutical provided us with a strong scientific rationale for evaluating MN-001 as an oral treatment for IC. MN-001 has been shown to block a number of the inflammatory mechanisms activated by mast cell degranulation that are important in the pathogenesis of inflammatory disorders, including IC and asthma (*e.g.*, leukotriene receptor antagonism and inhibition of phosphodiesterases III and IV, 5-lipoxygenase, phospholipase C and thromboxane A2). In addition, MN-001 produced anti-inflammatory effects in a variety of rodent models of IC and asthma; in these models, MN-001 reduced bladder hyper-reactivity much in the same way that it reduced airway