

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)

**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**  
(State or Other Jurisdiction of Incorporation

**33-0927979**  
(I.R.S. Employer Identification No.)

or Organization)

**4350 La Jolla Village Drive, Suite 950, San Diego, CA**  
(Address of Principal Executive Offices)

**92122**  
(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**  
Common Stock, par value \$0.001 per share

**Name of Each Exchange on Which Registered**  
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

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

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

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

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

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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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately \$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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The MediciNova logo is a registered trademark of MediciNova, Inc. All other product and company names are registered trademarks or trademarks of their respective companies.

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*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**

<b>Candidate</b>	<b>Disease/Indication</b>	<b>Phase of Development</b>	<b>Licensor</b>	<b>Licensed Territory</b>
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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<b>Product</b>				
<b>Candidate</b>	<b>Disease/Indication</b>	<b>Phase of Development</b>	<b>Licensor</b>	<b>Licensed Territory</b>
MN-166	CNS disorders**	<p>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.</p> <p>Phase 2 clinical trial completed in the second quarter of 2008.</p> <p>Prototype once-per-day oral formulation developed for future clinical trials</p> <p>Phase 1b/2a clinical trial in diabetic neuropathic pain completed in the fourth quarter of 2007</p> <p>Phase 1b National Institute on Drug Abuse, or NIDA, funded clinical trial in methamphetamine-dependent volunteers initiated in the fourth quarter of 2010</p> <p>Phase 1b/2a NIDA funded clinical trial to evaluate safety and efficacy in heroin-dependent volunteers completed in the fourth quarter of 2010</p> <p>Investigator initiated Phase 2 clinical trial collaboration with a headache and pain specialist in Australia initiated in the third quarter of 2011</p>	<p>Kyorin Pharmaceutical (MN-166)</p>	<p>Worldwide, except Japan, China, Taiwan and South Korea (MN-166)</p>





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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:

<b>Product</b>				
<b>Candidate</b>	<b>Disease/Indication</b>	<b>Phase of Development</b>	<b>Licensors</b>	<b>Licensed Territory</b>
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  $\beta_2$ -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  $\beta_2$ -adrenergic receptor. In these studies, the  $\beta_1$ -adrenergic receptor stimulating activity of MN-221 was less than that of other  $\beta_2$ -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  $\beta_2$ -adrenergic receptor agonists on the heart via  $\beta_1$ -adrenergic receptors may be reduced with MN-221. *Some in vitro* studies also suggested that MN-221 may act as only a partial  $\beta_1$ -adrenergic receptor agonist in cardiac tissue, while acting as a full  $\beta_2$ -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  $\beta_2$ -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,

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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<sub>1</sub>, 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<sub>1</sub> 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<sub>1</sub> 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<sub>1</sub> 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  $\beta_2$ -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<sub>1</sub>. FEV<sub>1</sub> 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<sub>1</sub> 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<sub>1</sub> 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<sub>1</sub> 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<sub>1</sub> 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<sub>1</sub>. 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  $\beta_2$ -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  $\beta_2$ -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  $\beta_2$ -adrenergic receptor agonists due to its greater selectivity for the  $\beta_2$ -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<sub>1</sub> (L) as compared to the baseline and placebo. At the end of the one hour infusion, FEV<sub>1</sub> (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 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.

### *Ibutilast (MN-166)*

The Ibutilast 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. Ibutilast 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-1 $\beta$ , TNF- $\alpha$ , 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, ibutilast, which was first approved in Japan more than 20 years ago. Ibutilast 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 ibutilast 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 ibutilast 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 ibutilast 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.

Ibutilast 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 ibutilast in the treatment of chronic medication overuse headache (MOH) pain is also ongoing in Australia and involves placebo or ibutilast administration for up to two months.

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*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-1 $\beta$ , TNF- $\alpha$  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- $\alpha$  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<sub>1</sub> 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<sub>1</sub>, 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*

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*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 hyper-reactivity in the lung.

*Clinical Results of MN-001 for Interstitial Cystitis.* We conducted a randomized, double-blind, placebo-controlled multi-center Phase 2 clinical trial in patients with moderate-to-severe IC, which was completed in the first quarter of 2007. This clinical trial involved 305 patients at 37 clinical sites in the U.S. Results from this clinical trial indicated that, while well-tolerated, MN-001 did not show a statistically significant clinical benefit compared to placebo on the primary endpoint (to be much or very much improved overall on a patient-rated global response assessment) at the doses tested in this clinical trial (500 mg once or twice a day for eight weeks). Results from this clinical trial also indicated that IC patients were more than twice as likely to respond on 500 mg of MN-001 administered twice a day compared to placebo (25 percent compared to 12 percent, p-value=0.04) after four weeks of treatment. This difference, however, was not observed at eight weeks due to continued improvement among placebo-treated patients. The response rate of patients treated with 500 mg of MN-001 once a day did not significantly differ from placebo at either four or eight weeks.

### *MN-029 for Solid Tumors*

*Indication Overview and Market Opportunity.* The American Cancer Society estimates that more than 1.5 million Americans were diagnosed with cancer in 2010, of which more than 750,000 patients were diagnosed with lung, prostate, colon, rectum or breast solid tumor cancers. The American Cancer Society also estimates that approximately 569,000 patients were ultimately to die from cancer in 2010. According to IMS Health, the global market for oncology products exceeded \$48.0 billion in 2008.

Tumor blood vessels are a promising target for cancer therapy. Compounds that act to deprive tumors of their blood supply fall into two classes: angiogenesis inhibitors and vascular disrupting agents, or VDAs. Angiogenesis inhibitors block the formation of new blood vessels formed in response to tumor growth, whereas VDAs disrupt blood flow through existing tumor blood vessels. We believe that VDAs have a potential advantage over angiogenesis inhibitors because VDAs work on existing tumor blood vessels and can kill hundreds of cancer cells that depend on that blood supply with even a brief interruption in blood flow, rather than simply slowing tumor growth by blocking new blood vessel formation.

*Overview of MN-029.* MN-029 is a novel, small molecule VDA being developed for the treatment of solid tumors. We licensed MN-029 from Angiogene Pharmaceuticals in June 2002. Several preclinical pharmacology studies conducted by Angiogene Pharmaceuticals and us have assessed the mechanism of action and anti-tumor activity of MN-029 *in vivo* in rodent models of breast adenocarcinoma, colon carcinoma, lung carcinoma and KHT sarcoma. In these studies, MN-029 damaged poorly formed tumor blood vessels by weakening tumor blood vessel walls and causing leakage, clotting and eventual vascular shutdown within the tumor. These studies suggest that MN-029 acts quickly and is rapidly cleared from the body, which may reduce the potential for some adverse effects commonly associated with chemotherapy. Shutdown of tumor blood flow in tumor models was confirmed through the use of dynamic contrast-enhanced magnetic resonance imaging, or DCE-MRI.





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*Clinical Results of MN-029 for Solid Tumors.* To date, we have conducted two Phase 1 clinical trials of MN-029 for the treatment of solid tumors, which completed in 2006 and 2007, respectively.

In the first Phase 1 clinical trial, MN-029 was administered as an intravenous infusion once every three weeks. Results from this clinical trial showed that MN-029 was well tolerated at doses that reduced tumor blood flow. A maximum tolerated dose of 180 mg/m<sup>2</sup> per dose was established in this clinical trial. The most common side effects of MN-029 were characteristic of other VDAs and included nausea, vomiting, fatigue and diarrhea. Nine of 34 patients with advanced solid tumors for whom no standard therapy was available had stable disease after three cycles of treatment. Six patients had prolonged (greater than six months) stable disease. Although no patients showed objective responses based on Response Evaluation Criteria in Solid Tumors, or RECIST criteria, which is tumor length on computed tomography, or CT, or MRI scans, semi-automated measurements of tumor volumes from CT scans showed a measureable reduction in tumor burden in the subject with the largest reduction in tumor blood flow (Ktrans -40 percent). Tumor blood flow reduction assessed by dynamic contrast-enhanced magnetic resonance imaging, or DCE-MRI, was recorded at doses greater than or equal to 120 mg/m<sup>2</sup>.

In the second Phase 1 clinical trial, MN-029 was administered as an intravenous infusion every seven days (days 1, 8, 15) followed by a 13-day recovery period (one cycle). Results from this clinical trial showed that MN-029 was well tolerated. The maximum dose was limited to 180 mg/m<sup>2</sup> per dose based on the results of the other Phase 1 trial that employed a less aggressive dosing schedule. The most common side effects of MN-029 in this clinical trial included nausea, vomiting, arthralgia and headache. Eleven of 20 patients with advanced solid tumors for whom no standard therapy was available had stable disease after two cycles of treatment. Four subjects continued on extended cycles of MN-029 treatment. Based on RECIST criteria, one patient with metastatic pancreatic cancer had an overall partial response with a duration of 74 days. Seven patients had stable disease with a median duration of 83 days.

### *MN-305 for Generalized Anxiety Disorder/Insomnia*

*Indication Overview and Market Opportunity.* The essential characteristic of generalized anxiety disorder is excessive, uncontrollable worry about everyday events. This constant worry affects daily functioning and can cause severe physical symptoms. Generalized anxiety disorder can occur with other anxiety disorders, depressive disorders or substance abuse. Generalized anxiety disorder is often difficult to diagnose because it is not triggered by a specific object or situation. The intensity, duration and frequency of the worry are disproportionate to the issue. As a result, generalized anxiety disorder tends to interfere with the patient's performance of tasks and ability to concentrate. According to the National Institute of Mental Health, anxiety disorders affect approximately 40 million American adults, of whom approximately 6.8 million suffer from generalized anxiety disorder. Anxiety disorders are the most prevalent of neuropsychiatric conditions, yet are generally considered to be under-diagnosed and therefore undertreated. Therefore, we believe that there is a significant opportunity for the introduction of new anxiety reducing drugs.

A variety of pharmacologic agents are used to manage patients with anxiety disorders. Benzodiazepines have been the mainstay of the treatment of acute anxiety since the late 1960s. However, their efficacy as a treatment has been limited by problems faced in chronic use due to their sedative effects. In the late 1980s, buspirone was introduced and widely used even though it takes effect slowly. Buspirone was well tolerated and relatively safe. During the late 1990s, newer anti-depressants, notably the specific serotonin reuptake inhibitors, or SSRIs, were increasingly used to treat anxiety as well. While effective, the use of SSRIs may result in a variety of undesirable side effects, including agitation and sexual dysfunction. Also, SSRIs may take weeks to exert their beneficial effects.

*Overview of MN-305 for Generalized Anxiety Disorder/Insomnia.* MN-305 is a serotonin receptor agonist with high affinity and selectivity for the serotonin 5-HT<sub>1A</sub> receptor subtype. Drugs that act through this mechanism, such as buspirone, have been proven to be clinically effective in treating generalized anxiety disorder. We licensed MN-305 from Mitsubishi Pharma Corporation, now Mitsubishi Tanabe Pharma



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Corporation, in April 2004. MN-305 has been shown to be more potent than buspirone and to exhibit anti-anxiety efficacy in a wide range of preclinical rodent models. For example, in a social interaction test, MN-305 prolonged the duration of social interaction in rats. Preclinical and clinical studies conducted by Mitsubishi Tanabe Pharma Corporation and us also suggest that MN-305 may have a more rapid onset of action than buspirone.

*Clinical Results of MN-305 for Generalized Anxiety Disorder/Insomnia.* Preliminary evidence of anti-anxiety efficacy was provided by a six-week, open-label, fixed-flexible dose Phase 2 clinical trial conducted by Mitsubishi Tanabe Pharma Corporation in Japan in 61 patients with neurotic disorders. The neurotic disorders included generalized anxiety disorder, panic disorder, agoraphobia, mixed anxiety and depressive disorder and dysthymia. MN-305 was well tolerated, with headaches being the most common side effect in this clinical trial. At the end of the clinical trial, the mean Hamilton Rating Scale for Anxiety score, or HAM-A score, which is a scale used to measure the intensity of anxiety symptoms, was reduced compared to the pre-treatment value. Similarly, a majority of the patients were rated Moderately Improved or better following treatment with MN-305. In addition, MN-305 was well tolerated in several clinical trials conducted by Mitsubishi Tanabe Pharma Corporation in healthy volunteers and patients with anxiety disorders and Major Depressive Disorder. These studies did not evaluate the reduction of anxiety symptoms in patients that were not treated with MN-305.

The IND for MN-305 was transferred to us from Mitsubishi Tanabe Pharma Corporation, which enabled us to conduct a Phase 2 randomized, double-blind, placebo-controlled clinical trial in 416 patients with generalized anxiety disorder, which was completed in the second quarter of 2006. The results revealed trends for improvement in all efficacy outcome measures. Statistically significant improvements in the total HAM-A score and in anxious mood, which is item 1 of the HAM-A score and was a secondary endpoint in this clinical trial, were observed through eight weeks of treatment. However, statistical significance on change from baseline of the total HAM-A score after ten weeks of treatment, which was the primary outcome measure of this clinical trial, was not achieved. MN-305 was well tolerated at all doses in this clinical trial, and we believe the findings were sufficiently positive to warrant further clinical evaluation of this product candidate.

We analyzed the results from our Phase 2 clinical trial of MN-305 in generalized anxiety disorder and performed in-depth analyses of subgroups that showed statistically significant improvement in certain aspects of the HAM-A score (e.g., insomnia). Based on these analyses, we initiated a Phase 2 proof-of-concept clinical trial of MN-305 for the treatment of insomnia in the first quarter of 2007 to assess the effects of three dosages of MN-305 (1 mg, 3 mg and 6 mg) and placebo, all administered orally approximately 60 minutes before bedtime. This clinical trial, which involved 74 subjects at ten study centers in the U.S., was completed in the fourth quarter of 2007. This clinical trial failed to achieve statistical significance in its primary endpoint of reducing Wake (time) After Sleep Onset, or WASO. MN-305 was well tolerated in this clinical trial with no clinically significant adverse events observed at any dose tested, and there was no evidence of any decrements in psychomotor performance, as assessed in digit symbol substitution and symbol copying tests, in patients treated with MN-305. Based upon the results of this clinical trial, we decided to terminate the evaluation of MN-305 for the treatment of insomnia.

#### *MN-221 for Preterm Labor*

*Indication Overview and Market Opportunity.* Preterm labor is caused by the onset of uterine contractions before term. According to a November 2002 publication in Obstetrics & Gynecology, preterm labor is the leading cause of neonatal mortality and a substantial portion of all birth-related short and long-term morbidity. Successful inhibition of premature birth is known to reduce the risk of complications. Despite extensive research into preterm labor during the past several decades, the rate of premature births has not decreased. According to the National Vital Statistics Reports issued by the U.S. Department of Health and Human Services, or DHHS, there were 4.3 million births in the U.S. in 2007. The 2007 preterm birth rate was 12.7 percent. The DHHS estimates that the costs associated with preterm births are over \$26 billion annually. According to the World Health Organization, six percent to seven percent of all births in Europe occur before term.

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Currently, therapy for preterm labor remains targeted at uterine contractions.  $\beta_2$ -adrenergic receptor agonists are generally used as first-line treatments for premature labor. The only FDA-approved treatment for preterm labor is ritodrine, a  $\beta_2$  agonist. However, ritodrine has not been available for sale in the U.S. market since 1999. The more widely used treatment for preterm labor is another  $\beta_2$  agonist, terbutaline; however, this drug is not approved by the FDA for preterm labor. Atosiban, an oxytocin antagonist, is available in Europe, but was denied regulatory approval in the U.S. The usefulness of these  $\beta_2$ -adrenergic receptor agonists is often limited by the adverse reactions they produce, which include cardiovascular side effects such as heart palpitations. As a result, we believe that there is a need for treatments with better safety and tolerability profiles that are effective in reducing the premature birth rate and/or providing for longer gestation.

*Overview of MN-221 for Preterm Labor.* MN-221 is highly-selective  $\beta_2$ -adrenergic receptor agonist being developed for the treatment of preterm labor. We licensed MN-221 from Kissei Pharmaceutical in February 2004. Preclinical testing *in vitro* and *in vivo* showed MN-221 to be more selective for the  $\beta_2$ -adrenergic receptor than other  $\beta_2$ -adrenergic receptor agonists currently used to treat preterm labor. Moreover, *in vitro* studies also suggested that MN-221 may act as only a partial  $\beta_1$ -adrenergic receptor agonist in cardiac tissue, while acting as a full  $\beta_2$ -adrenergic receptor in the uterus. This improved receptor binding and functional selectivity may result in fewer cardiovascular side effects than are commonly observed with other  $\beta_2$ -adrenergic receptor agonists used to treat this condition. In preclinical pharmacology studies in pregnant rats and sheep conducted by Kissei Pharmaceutical, MN-221 reduced the number of spontaneous or drug-induced uterine contractions. Furthermore, in these studies, MN-221 delayed both normal and preterm labor in rats and caused a marked increase in the bodyweight of rat pups as a result of prevention of premature birth. In rat and sheep studies which compared MN-221 to ritodrine and/or terbutaline, the potency of MN-221 was greater than those  $\beta_2$ -adrenergic receptor agonists.

*Clinical Results of MN-221 for Preterm Labor.* To date, pharmacokinetic and safety data has been generated from human experience with MN-221 through Phase 1 clinical studies in healthy male and non-pregnant female volunteers conducted by Kissei Pharmaceutical in Japan and the United Kingdom and a Phase 1 clinical trial in the U.S. conducted by us. A total of 244 healthy subjects received intravenous infusions of either MN-221 or a placebo. MN-221 was generally well tolerated. A pilot double-blind, placebo-controlled Phase 2 clinical trial of MN-221 was completed in 2004 by Kissei Pharmaceutical in seven women in preterm labor in the United Kingdom. A trend towards a reduction in the number of uterine contractions was observed in MN-221-treated women and, as a result, only limited conclusions could be drawn from this clinical trial. No serious adverse events related to MN-221 were observed in this clinical trial.

We initiated a Phase 1 clinical trial in healthy pregnant women in the third quarter of 2006. Ten healthy, pregnant volunteers who were not in labor participated in this clinical trial, which was completed in the second quarter of 2007. The volunteers received a single-dose intravenous infusion regimen of MN-221, consisting of two consecutive rounds of a 15-minute priming and a 105-minute maintenance infusion to deliver 294 micrograms of MN-221 over four hours. The primary objectives of this clinical trial were to determine the pharmacokinetics, safety and tolerability of this infusion regimen of MN-221 in pregnant women. No significant safety concerns with MN-221 were identified in this clinical trial.

### *MN-246 for Urinary Incontinence*

*Indication Overview and Market Opportunity.* Urinary incontinence occurs when normal regulation of bladder function is lost. According to the DHHS, there are over 13 million adults in the U.S. suffering from urinary incontinence.

The market for drugs to treat urinary incontinence is expected to grow substantially as more patients seek treatment and as newer drugs are introduced to the market. According to GlobalData, the global market for urinary incontinence was \$2.5 billion in 2009 and is projected to grow to \$3.4 billion by 2017. The current marketplace is dominated by anti-cholinergic drugs that are modestly effective and produce

treatment-limiting

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side effects such as dry mouth. According to Pfizer Inc.'s 2009 annual report, sales of its Detro<sup>®</sup> were approximately \$1.2 billion in 2009.

*Overview of MN-246 for Urinary Incontinence.* MN-246 is a novel  $\beta_3$ -adrenergic receptor agonist being developed for the treatment of urinary incontinence. We licensed MN-246 from Mitsubishi Pharma Corporation, now Mitsubishi Tanabe Pharma Corporation, in December 2004. We believe that MN-246 represents a new approach to treating urinary incontinence and may have advantages over existing therapies, including potential improvements in efficacy through increases in bladder volume with decreases in involuntary bladder contractions and the absence of anti-cholinergic side effects, such as dry mouth. In preclinical studies in rats conducted by Mitsubishi Tanabe Pharma Corporation, MN-246 was more potent and active than oxybutynin and propiverine in increasing bladder volume. In addition, the studies showed that MN-246 produced little or no increase in residual urine volume and no anti-cholinergic side effects in rats. MN-246 also increased bladder volume in preclinical studies conducted on dogs and monkeys.

*Clinical Results of MN-246 for Urinary Incontinence.* We completed a double-blind, randomized, placebo-controlled, single escalating dose Phase 1 clinical trial of MN-246 for the treatment of urinary incontinence in healthy volunteers to evaluate the safety, tolerability and pharmacokinetics of MN-246 in the fourth quarter of 2006. We also conducted a Phase 1 food effects study in healthy volunteers, which was completed in the first quarter of 2007. MN-246 was tolerated in both clinical trials.

#### *MN-447 and MN-462 for Thrombotic Disorders*

*Indication Overview and Market Opportunity.* Despite advances in the treatment of cardiovascular disease, or CVD, more than 616,000 people died of heart disease in 2007, according to the CDC's National Vital Statistics Reports. Heart disease causes approximately 25% of deaths in the U.S. According to the American Heart Association, there are 80 million individuals in the U.S. that currently live with some form of CVD, which can include high blood pressure, coronary heart disease, stroke, angina (chest pain), myocardial infarction (heart attack) and congenital heart defects. According to Datamonitor, worldwide sales of antithrombotic drugs are forecasted to reach approximately \$22 billion in 2017. We believe that there remains an unmet medical need for safe and effective treatments for thrombotic conditions, including acute coronary syndrome, myocardial infarction, peripheral arterial disease and percutaneous coronary interventions.

According to the CDC, CVD remains the leading cause of death in the U.S. for both men and women. Given the high mortality and morbidity rates associated with CVD. We believe there is an urgent need for more targeted therapies that can intervene in known molecular pathways and minimize damage to the heart and related tissues.

*Overview of MN-447 and MN-462 for Thrombotic Disorders.* MN-447 and MN-462 are novel, small molecule antithrombotic agents being developed for the treatment of various thrombotic disorders. We licensed MN-447 and MN-462 from Meiji Seika Kaisha in November 2006.

MN-447 is a cardioprotective, anti-platelet agent that acts as a dual antagonist of glycoprotein, or GP, IIb/IIIa and integrin  $\alpha_v\beta_3$ , receptors that play key roles in blood clot formation and various cell behaviors and functions such as leukocyte adhesion. Preclinical studies have demonstrated that MN-447 acts downstream by inhibiting the final common pathway of platelet aggregation—the cross-linking of platelets via fibrinogen bridges to GP IIb/IIIa receptors. Inhibition of integrin  $\alpha_v\beta_3$  receptors has been linked to an inhibition of leukocyte adhesion to endothelium (the layer of cells lining blood vessels), reduction of hyperplasia (abnormal cellular proliferation) and lumen stenosis (blood vessel constriction) in response to vascular injury. In animal models of myocardial infarction and unstable angina, the dual inhibitory activity of MN-447 produced superior cardioprotective efficacy, such as reduction in infarct size after reperfusion (restoration of blood flow) compared to inhibition of the GP IIb/IIIa receptor alone, and showed a low risk of bleeding.

MN-462 is a selective inhibitor of a key enzyme in the intrinsic antifibrinolytic mechanism, plasma carboxypeptidase B, or CPB, and also called activated thrombin-activatable fibrinolysis inhibitor, or TAFIa.



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which inhibits physiological fibrinolysis, or the lysis or dissolving of blood clots. By enhancing intrinsic fibrinolysis through plasma CPB inhibition, MN-462 has the potential to reduce and prevent thrombus or blood clot formation, as well as dissolve formed thrombus. In preclinical studies, MN-462 demonstrated significant fibrinolytic-enhancing and anti-thrombotic activities as monotherapy in several thrombosis models, as well as activities when used as an adjunct to fibrinolytics such as tissue plasminogen activator, or t-PA. The effect of MN-462 in enhancing the intrinsic fibrinolytic process was also observed to result in a low risk of bleeding.

## **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 successfully 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.

Pursuant to the terms of our license agreement with Kissei Pharmaceutical for MN-221, Kissei Pharmaceutical has the exclusive right to manufacture the commercial supply of the API for MN-221. If we enter into a supply agreement with Kissei Pharmaceutical, we will purchase from Kissei Pharmaceutical 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 any agreement established regarding the commercial supply of MN-221 in standard vials or for the API or finished product of any of our product candidates.

For the ibudilast development program, we have sourced and imported delayed-release ibudilast capsules, marketed in Japan as Pinatos<sup>®</sup>, from Taisho-Teva Pharmaceuticals. We are not currently developing our own formulation and will determine our long-term drug supply strategy in tandem with significant development progress in our program.

## **Intellectual Property and License Agreements**

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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

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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 170 issued and pending foreign patents and applications corresponding to these U.S. patents and patent applications. In addition to these licensed rights, we hold 13 issued U.S. patents and have filed 15 additional U.S. patent applications. We also hold 59 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-221*

On February 25, 2004, we entered into an exclusive license agreement with Kissei Pharmaceutical for the development and commercialization of MN-221. Kissei 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), 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 Pharmaceutical. 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.

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 Pharmaceutical during the development phase and 180 days' prior written notice to Kissei Pharmaceutical 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 Pharmaceutical 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 Pharmaceutical \$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-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.

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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

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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.

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.

In addition, we own, co-own or hold licenses to five issued U.S. patents and nine pending U.S. patent applications as well as corresponding pending foreign patent applications. 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 analogs.

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 ibudilast (MN-166) for the treatment of progressive forms of multiple sclerosis. A patent maturing from this allowed patent application is expected to expire no earlier than early 2029 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. We are pursuing counterparts of this patent application in certain foreign jurisdictions. We have received an additional Notice of Allowance for a pending patent application which covers the use of ibudilast (MN-166) for the treatment of neuropathic pain in Japan.

### *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 one U.S. patent and certain corresponding patents and patent applications 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.

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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, 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.

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. 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 on January 14, 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.



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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.

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, including MN-246, processes for the production of such phenylethanolamines, a pharmaceutical composition of such phenylethanolamines and methods of use for such

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phenylethanolamines for the treatment of a variety of human or animal ailments, including accelerated or spasmodic gastrointestinal motility, dysuria, pollakisuria, urinary incontinence, obesity and diabetes. This U.S. patent is set to expire on October 24, 2016. Foreign

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counterparts have been patented in other countries and are also set to expire no earlier than October 24, 2016. 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-246 to develop products incorporating the MN-246 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.

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-246 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-246 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 \$750,000 to date, and we are obligated to make payments of up to \$14.5 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-447*

On November 1, 2006, we entered into an exclusive license agreement with Meiji Seika Kaisha for the development and commercialization of MN-447. Meiji Seika Kaisha 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, Bangladesh, Brunei, Cambodia, People's Republic of China, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam), sub-licensable license from Meiji Seika Kaisha for MN-447 (and any other compound claimed or covered by U.S. patent 6,420,558) for any human use. This license includes an exclusive sub-licensable license under one U.S. patent and certain corresponding patents in foreign countries. The U.S. patent covering MN-447 and methods of treating an integrin  $\alpha\beta 3$ -mediated disease, platelet thrombosis, aggregation and related disorders, which issued on July 16, 2002, is set to expire on April 9, 2019. Patent applications corresponding to this U.S. patent were granted in certain foreign countries. Under the terms of the license, we granted a license to Meiji Seika Kaisha to use our know-how and patents relating to MN-447 to develop products incorporating the MN-447 compound outside of our territory.

This license agreement may be terminated by either party following an uncured breach of any material provision of the agreement by the other party upon 90 days' written notice or the inability or delay in performing under the agreement due to a force majeure event which lasts longer than 12 months. We also have the right to terminate the agreement in the event of third party intellectual property claims which are not timely remedied by us and Meiji Seika Kaisha or if, in our reasonable opinion, the safety, patient tolerability, efficacy, profile or commercial viability of MN-447 does not justify continued development. Meiji Seika Kaisha also has the right to terminate the agreement in the event that we cease development of MN-447 for a period of one year or longer.

The term of the agreement is determined on a country-by-country basis and extends until the expiration of the last Meiji Seika Kaisha 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 15 years from the date of first commercial sale, 15 years from the date of first commercial sale.

Under the license agreement, we have paid Meiji Seika Kaisha \$400,000 to date, and we are obligated to make payments of up to \$8.7 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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*MN-462*

On November 1, 2006, we entered into an exclusive license agreement with Meiji Seika Kaisha for the development and commercialization of MN-462. We obtained an exclusive, worldwide (excluding Japan, Bangladesh, Brunei, Cambodia, People's Republic of China, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam), sub-licensable license from Meiji Seika Kaisha for MN-462 (and any other compound claimed or covered by U.S. patent 6,576,627) for any human use. This license includes an exclusive sub-licensable license under certain corresponding patents in foreign countries. The U.S. patent covering MN-462 medicament compositions containing MN-462, and methods of therapeutic treatment or preventive treatment of thrombotic disease, which issued on June 10, 2003, is set to expire on September 13, 2020. Patent applications corresponding to this U.S. patent were granted in certain foreign countries. Under the terms of the license, we granted a license to Meiji Seika Kaisha to use our know-how and patents relating to MN-462 to develop products incorporating the MN-462 compound outside of our territory.

This license agreement may be terminated by either party following an uncured breach of any material provision of the agreement by the other party upon 90 days' written notice or the inability or delay in performing under the agreement due to a force majeure event which lasts longer than 12 months. We also have the right to terminate the agreement in the event of third party intellectual property claims which are not timely remedied by us and Meiji Seika Kaisha or if, in our reasonable opinion, the safety, patient tolerability, efficacy, profile or commercial viability of MN-462 does not justify continued development. Meiji Seika Kaisha also has the right to terminate the agreement in the event that we cease development of MN-462 for a period of one year or longer.

The term of the agreement is determined on a country-by-country basis and extends until the expiration of the last Meiji Seika Kaisha 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 15 years from the date of first commercial sale, 15 years from the date of first commercial sale.

Under this license agreement, we have paid Meiji Seika Kaisha \$400,000 to date, and we are obligated to make payments of up to \$8.7 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.

*General*

Our proposed commercial activities may conflict with patents which have been or may be granted to competitors, universities and/or others. Third parties could bring legal action against us, our licensors or our sub-licensees claiming patent infringement and could seek damages or enjoin manufacturing and marketing of the affected product or its use or the use of a process for the manufacturing of such products. If any such actions were to be successful, in addition to any potential liability for indemnification, damages and attorneys' fees in certain cases, we could be required to obtain a license, which may not be available on commercially reasonable terms or at all, in order to continue to manufacture, use or market the affected product. We also rely upon unpatented proprietary technology because, in some cases, our interests would be better served by reliance on trade secrets or confidentiality agreements than by patents. However, others may independently develop substantially equivalent proprietary information and techniques or gain access to or disclose such proprietary technology. We may not be able to meaningfully protect our rights in such unpatented proprietary technology. We may also conduct research on other pharmaceutical compounds or technologies, the rights to which may be held by, or be subject to patent rights of, third parties. Accordingly, if products based on such research are commercialized, such commercial activities may infringe patents or other rights, which may require us to obtain a license to such patents or other rights. We are not aware of any third-party infringements of patents we hold or licenses and have not received any material claims by third parties of infringement by us of such parties' intellectual property rights.



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There can be no assurance that patent applications filed by us or others, in which we have an interest as assignee, licensee or prospective licensee, will result in patents being issued or that, if issued, any of such patents will afford protection against competitors with similar technology or products or could not be circumvented or challenged. For example, we have U.S. patents covering the method of using MN-166 to treat MS and the method of using MN-166 to treat neuropathic pain, but we do not have any composition of matter patent claims for MN-166. As a result, unrelated third parties may develop products with the same API as MN-166 so long as such parties do not infringe our method of use patent, other patents we have exclusive rights to through our licensor or any patents we may obtain for MN-166.

In addition, if we develop certain products that are not covered by any patents, we will be dependent on obtaining market exclusivity under the data exclusivity provisions of Hatch-Waxman Act for such products. If we are unable to obtain strong proprietary rights protection for our products after obtaining regulatory approval, competitors may be able to market competing generic products by taking advantage of an abbreviated procedure for obtaining regulatory clearance, including the ability to demonstrate bioequivalency to our product(s) without being required to conduct lengthy clinical trials. Certain of our license agreements provide for reduced royalties or, in some cases, foregone royalties in the event of generic competition.

## **Competition**

The development and commercialization of new drugs is extremely competitive and characterized by extensive research efforts and rapid technological progress. Competition in our industry occurs on a variety of fronts, including developing and bringing new products to market before others, developing new products to provide the same benefits as existing products at lower cost and developing new products to provide benefits superior to those of existing products. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, in the U.S. and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our product development programs. Many of our competitors have products that have been approved or are in advanced development and may succeed in developing drugs that are more effective, safer and more affordable or more easily administered than ours or that achieve patent protection or commercialization sooner than our products. Our competitors may also develop alternative therapies that could further limit the market for any products that we are able to obtain approval for, if at all.

In many of our target disease areas, potential competitors are working to develop new compounds with different mechanisms of action and attractive efficacy and safety profiles. Many of our competitors have substantially greater financial, research and development resources (including personnel and technology), clinical trial experience, manufacturing, sales and marketing capabilities and production facilities than we do. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies.

### *MN-221 for Acute Exacerbations of Asthma*

Our MN-221 product candidate is being developed for the treatment of acute exacerbations of asthma in the emergency room setting. The current standard of care for acute exacerbations of asthma is inhaled albuterol (a  $\beta_2$ -adrenergic receptor agonist), inhaled ipratropium (an anticholinergic) and oral or injected corticosteroids. In addition, subcutaneously administered terbutaline (a  $\beta_2$ -adrenergic receptor agonist) is sometimes used to treat this condition, particularly in pediatric patients. Certain oral anti-inflammatory asthma drugs are being investigated in an intravenous form for the treatment of acute exacerbations of asthma.

### *MN-221 for Chronic Obstructive Pulmonary Disease Exacerbations*

Our MN-221 product candidate is also being developed for the treatment of COPD exacerbations. The standard of care for COPD exacerbations is similar to that of acute exacerbations of asthma in that inhaled



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bronchodilators and anticholinergics are administered; however, antibiotics are also administered and parenteral terbutaline is excluded because of the exclusively adult patient population. A greater percentage of patients diagnosed with COPD exacerbations are hospitalized than patients diagnosed with asthma exacerbations, and such patients continue the same treatment paradigm as in the emergency department.

### *MN-166 for Multiple Sclerosis*

Our MN-166 product candidate is pending development for the treatment of progressive MS. Only one drug, mitoxantrone, is approved for treating this disease. *MN-166 for Other Central Nervous System Disorders*

Our MN-166 product candidate has been in development for treatment of neuropathic pain and opioid withdrawal and methamphetamine addiction. Current treatments for neuropathic pain include anti-epileptics such as Pfizer Inc.'s Neurontin® (gabapentin) and Lyrica® (pregabalin), and antidepressants, including Eli Lilly & Co.'s Cymbalta® (duloxetine). We are aware of additional compounds for chronic neuropathic pain that are currently in development at numerous companies including GlaxoSmithKline plc, Pfizer Inc., Cognetix, Inc., GW Pharmaceuticals plc, Endo Pharmaceuticals Holdings Inc., Avanir Pharmaceuticals, Pain Therapeutics, Inc., and XenoPort, Inc.

Current treatments for withdrawal symptoms include narcotics such as generic methadone and Reckitt Benckiser Pharmaceuticals, Inc.'s Suboxone® (buprenorphine) and Subutex® (buprenorphine + the narcotic antagonist naloxone). Limited non-narcotic drug candidates for withdrawal symptoms exist. Britannia Pharmaceuticals Limited's BritLofex® (Lofexidine), licensed for development in U.S. clinical trials to US WorldMeds LLC, is an alpha adrenoceptor agonist like clonidine which may have somewhat less orthostatic hypotension limitations. Vigabatrin (Sabril®), a re-directed anti-epileptic drug, is in Phase 2 development for cocaine and methamphetamine dependence by Catalyst Pharmaceutical Partners.

### *MN-001 for Bronchial Asthma*

Our MN-001 product candidate has been in development for the treatment of bronchial asthma. There are two currently marketed leukotriene inhibitors, Merck & Co. Inc.'s Singulair® (montelukast) and AstraZeneca PLC's Accolair® (zafirlukast).

### *MN-001 for Interstitial Cystitis*

Our MN-001 product candidate has been in development for the treatment of IC. There are two currently marketed products, Ortho-McNeil-Janssen Pharmaceuticals, Inc.'s/Teva Pharmaceuticals Industries Ltd.'s Elmiron® and Bioniche Pharma USA LLC's RIMSO-50®. Urigen Pharmaceuticals, Inc.'s URG101 for the treatment of painful bladder syndrome/interstitial cystitis is in Phase 2 clinical testing.

### *MN-029 for Solid Tumors*

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Our MN-029 product candidate has been in development for the treatment of solid tumors. There are a number of compounds in clinical development with a mechanism similar to MN-029, including Oxigene Inc.'s ZYBRESTAT (fosbretabulin) and Sanofi-Aventis' AVE 8062 (ombrabulin), which are in Phase 3 clinical testing.

### *MN-305 for General Anxiety Disorder*

Our MN-305 product candidate has been in development for the treatment of General Anxiety Disorder. There are a number of approved products to treat generalized anxiety disorder, including Eli Lilly and Company's Cymbalta® (duloxetine).

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### *MN-221 for Preterm Labor*

Our MN-221 product candidate has been in development for the treatment of preterm labor. An oxytocin antagonist on the market is Tractocile (atosiban). GlaxoSmithKline's atosiban is an oxytocin antagonist in Phase 2 development.

### *MN-246 for Urinary Incontinence*

Our MN-246 product candidate has been in development for the treatment of urinary incontinence. There are a number of compounds in various stages of clinical development to treat urinary incontinence. Pfizer Inc.'s Detrol/Detrol LA (tolterodine tartrate) is a market leader, and other marketed drugs include Astellas Pharma Inc.'s VESicare® (solifenacin succinate) and Novartis AG's Enablex® (darifenacin), both of which are anti-cholinergic agents. Ono Pharmaceutical Co., Ltd. and Kyorin Pharmaceutical have received approval for Staybla® (muscarinic antagonist). Pfizer Inc.'s Toviaz® (fesoterodine fumarate), another muscarinic antagonist, has also been approved. Astellas Pharma Inc. also has a  $\beta_3$ -adrenergic receptor agonist in development for the treatment of this indication (mirabegron).

### *MN-447 and MN-462 for Thrombotic Disorders*

Our MN-447 and MN-462 product candidates have been in development for the treatment of thrombotic disorders. Both product candidates are currently in preclinical development; therefore, we have not identified the particular thrombotic disorders that we intend to target upon reaching the clinical development stage for these product candidates. Consequently, we cannot accurately evaluate the competition we will face. Currently, the market leaders for anti-thrombotic drugs are Bristol-Myers Squibb Company's and Sanofi-Aventis' Plavix® (clopidogrel) and Sanofi-Aventis' Lovenox® (enoxaparin).

## **Government Regulation**

Government authorities in the U.S. and other countries extensively regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution, sampling, marketing and import and export of pharmaceutical products and biologics such as those we are developing. In the U.S., the FDA, under the Federal Food, Drug and Cosmetic Act, as amended, and other federal statutes and regulations, subjects pharmaceutical products to extensive and rigorous review. Any failure to comply with applicable requirements, both before and after approval, may subject us, our third-party manufacturers, contractors, suppliers and partners to administrative and judicial sanctions, such as a delay in approving or refusal to approve pending applications, fines, warning letters, product recalls, product seizures, total or partial suspension of manufacturing or marketing, injunctions and/or criminal prosecution.

### *U.S. Regulatory Approval*

*Overview.* In the U.S., drugs and drug testing are regulated by the FDA under the Federal Food, Drug and Cosmetic Act, as well as state and local government authorities. All of our product candidates in development will require regulatory approval by government agencies prior to commercialization. To obtain approval of a new product from the FDA, we must, among other requirements, submit data supporting safety and

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efficacy, as well as detailed information on the manufacture and composition of the product and proposed labeling. Our product candidates are in the early stages of testing and none has been approved. The steps required before a drug can be approved generally involve the following:

completion of preclinical laboratory and animal tests;

submission of an Investigational New Drug Application, or IND, which must become effective before human clinical trials may begin in the U.S.;

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completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each indication for which approval is sought;

submission to the FDA of an NDA accompanied by a substantial user fee;

development of manufacturing processes which conform to FDA-mandated commercial good manufacturing practices, or cGMPs, and satisfactory completion of FDA inspections to assess cGMP compliance and clinical investigator compliance with good clinical practices; and

FDA review and approval of an NDA, which process may involve input from advisory committees to the FDA and may include post-approval commitments for further clinical studies and distribution restrictions intended to mitigate drug risks.

The testing, collection of data, preparation of necessary applications and approval process requires substantial time, effort and financial resources. Additionally, statutes, rules, regulations and policies may change and new regulations may be issued that could delay such approvals. The FDA may not act quickly or favorably in reviewing our applications, and we may encounter significant difficulties and costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our products.

*Preclinical Tests.* Preclinical tests include laboratory evaluation of the product candidate, its chemistry, toxicity, formulation and stability, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the preclinical tests, together with manufacturing information, analytical data and other available information about the product candidate, are submitted to the FDA as part of an IND. Preclinical tests and studies can take several years to complete and, despite completion of those tests and studies, the FDA may not permit clinical testing to begin.

*The IND Process.* An IND must be effective to administer an investigational drug to humans. The IND will automatically become effective 30 days after its receipt by the FDA unless the FDA, before that time, places the IND on clinical hold. At any time thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold if the FDA deems it appropriate. In such case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin or continue. The IND application process may become extremely costly and substantially delay development of our products. Moreover, positive results in preclinical tests or prior human studies do not necessarily predict positive results in subsequent clinical trials.

*Clinical Trials.* Human clinical trials are typically conducted in three sequential phases that may overlap:

Phase 1: The drug is initially introduced into a small number of human subjects or patients and tested for safety, dosage tolerance, absorption, distribution, excretion and metabolism.

Phase 2: The drug is introduced into a limited patient population to assess the efficacy of the drug in specific, targeted indications, assess dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks.

Phase 3: The drug is introduced into an expanded patient population at geographically dispersed clinical trial sites to further evaluate clinical efficacy and safety.

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Prior to initiation of each clinical trial, an independent Institutional Review Board, or IRB, for each medical site proposing to conduct the clinical trials must review and approve the study protocol and study subjects must provide informed consent for participation in the study.

We cannot be certain that we will successfully complete Phase 1, 2 or 3 testing of our drug candidates within any specific time period, if at all. Clinical trials must be conducted in accordance with the FDA's good clinical practices requirements. The FDA may order the partial, temporary or permanent discontinuation of a

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clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The IRB may also require the clinical trial at that site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

*The NDA Process.* If clinical trials are successful, the next step in the drug regulatory approval process is the preparation and submission to the FDA of a NDA. The NDA is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical product for marketing and sale in the U.S. The NDA must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. A substantial user fee must also be paid with the submission of the NDA, unless an exemption applies.

Upon submission of the NDA, the FDA will make a threshold determination as to whether the application is sufficiently complete to permit review and, if not, will issue a refuse to file letter. If the submission is accepted for filing, the FDA begins an in-depth review of the NDA and will attempt to review and take action on the application in accordance with performance goals established in connection with the user fee laws. Among the conditions for a NDA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform on an ongoing basis with cGMPs.

If the FDA's evaluations of the NDA and the clinical and manufacturing procedures and facilities cGMPs are favorable, the FDA may issue either an approval letter or a complete response letter, which contains guidance on the conditions that must be met in order to secure approval of the NDA. If and when those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. The FDA may also grant approval with requirements to complete post-marketing studies, referred to as Phase 4 clinical trials, or restrictive product labeling, or may impose other restrictions on marketing or distribution, such as the adoption of a Risk Evaluation and Mitigation Strategy, or REMS. The FDA may deny or delay approval of applications that do not meet applicable regulatory criteria or if the FDA determines that the clinical data do not adequately establish the safety and efficacy of the drug.

*The Hatch-Waxman Act.* Under the Hatch-Waxman Act, certain newly approved drugs and indications benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act provides five-year marketing exclusivity to the first applicant to gain approval of an NDA for a new chemical entity, meaning that the FDA has not previously approved any other new drug containing the same active moiety. The Hatch-Waxman Act also provides three years of marketing exclusivity for the approval of new and supplemental NDAs for, among other things, new indications, dosages or strengths of an existing drug, if new clinical investigations that were conducted or sponsored by the applicant are essential to the approval of the application. Pediatric exclusivity of six months may also be available if agreement is reached with the FDA and qualifying studies of product candidates in pediatric populations are conducted.

*Manufacturing and Other Regulatory Requirements.* Both before and after approval, we and our third-party manufacturers must comply with a number of regulatory requirements. For example, if we seek to make certain changes to an approved product, such as promoting or labeling a product for a new indication, manufacturing changes or additional labeling claims, we will need FDA review and approval. Advertising and other promotional materials must comply with FDA requirements and established requirements applicable to drug samples. In addition, we may not label or promote the product for an indication that has not been approved by the FDA. Securing FDA approval for new indications or product enhancements and, in some cases, for new labeling claims, is generally a time-consuming and expensive process that may require us to conduct clinical trials under the FDA's IND regulations. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all. In addition, adverse experiences associated with use of the products must be reported to the FDA, and FDA rules govern how we can label, advertise or otherwise commercialize our products.

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The NDA holders and manufacturers of approved products will be subject to continual review and periodic inspections by the FDA and other authorities, where applicable, and must comply with ongoing requirements, including the FDA's cGMP requirements. Manufacturers must provide certain safety and efficacy information and make certain other required reports. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, record-keeping and other requirements. The FDA periodically inspects drug manufacturing facilities to evaluate compliance with cGMP requirements. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval. Because we intend to contract with third parties for manufacturing of our products, our ability to control third-party compliance with FDA requirements will be limited to contractual remedies and rights of inspection.

In addition to FDA restrictions on marketing of pharmaceutical products, several other state and federal laws have been applied to restrict certain sales and marketing practices in the pharmaceutical industry in recent years. These laws include licensing requirements, compliance program requirements, annual certificates and disclosures, anti-kickback statutes and false claims statutes. The federal Anti-Kickback Statute, prohibits knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid or other federally financed health care programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the Anti-Kickback Statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal health care programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Several pharmaceutical and other health care companies have been prosecuted under these laws for allegedly promoting their products for off-label uses, which in turn led to claims being submitted to and paid by the Medicare and Medicaid programs. The majority of states also have statutes or regulations similar to the Anti-Kickback Statute and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with our research.

### *Foreign Regulatory Approval*

We will have to complete approval processes, similar or related to the U.S. approval processes, in virtually every foreign market for our products in order to conduct clinical or preclinical research and to commercialize our drug candidates in those countries. The approval procedures and the time required for approvals vary from country to country and may involve additional testing. In addition, regulatory approval of prices is required in most countries other than the U.S. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or our collaborators.

Similar to the U.S. regulatory framework, the various phases of preclinical and clinical research are subject to significant regulatory controls within the European Union. Variations among national regimes exist. However, most jurisdictions require regulatory and ethics committees approval of interventional clinical trials. Most European regulators also require the submission of adverse event reports during a study and a copy of the final study report.





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Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or decentralized procedure. The centralized procedure is currently mandatory for products developed by means of a biotechnological process and optional for new active substances and other innovative medicinal products with novel characteristics. It provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit applications in other European Union member states, requesting them to mutually recognize the marketing authorization already granted. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize the existing approval.

Where possible, we will strive to choose the European regulatory filing route that will most rapidly enable us to obtain the needed regulatory approvals. However, the chosen regulatory strategy may not secure regulatory approvals or approvals of the chosen product indications. In addition, these approvals, if obtained, may take longer than anticipated.

## **Employees**

We have assembled an experienced and cohesive management and support team, with core competencies in general management, clinical development, regulatory affairs and corporate development. As of March 27, 2012, we had 14 full-time employees, following a reduction in force which took place in January 2011, wherein we down-sized the company to save costs. We believe that our relations with our employees are good, and we have no history of work stoppages.

## **Recent Developments**

### *Joint Venture*

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. In accordance with the joint venture agreement, on March 16, 2012, we paid \$650,000 for our 30% interest in the joint venture company. The other parties to the joint venture agreement are responsible for providing their initial funding in the joint venture company for their combined 70% interest, and for future funding for the joint venture company's activities. 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.

## **Company Information**

We were originally incorporated in the State of Delaware in September 2000. Our principal executive offices are located at 4350 La Jolla Village Drive, Suite 950, San Diego, CA 92122. Our telephone number is (858) 373 1500. Our website is [www.medicinova.com](http://www.medicinova.com), which includes links to reports we have filed with the Securities and Exchange Commission, or SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report on Form 10-K.



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### **Item 1A. Risk Factors**

*We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Annual Report on Form 10-K and our other public filings with the SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our results of operations and financial condition.*

#### **Risks Related to Our Business and Industry**

*We have incurred significant operating losses since our inception and expect that we will incur continued losses for the foreseeable future.*

We are a development stage biopharmaceutical company with a limited operating history. We have incurred significant net losses since our inception. For the year ended December 31, 2011, we had a net loss of approximately \$17.7 million and our accumulated deficit was approximately \$285.3 million. If we are successful in securing a strategic collaboration or in raising additional capital to support the expansion of our business, our annual net losses may increase over the next several years as we expand our infrastructure and incur significant costs related to the development of our product candidates.

If we have taxable income in the future, utilization of the net operating losses, or NOL, and tax credit carry-forwards will be subject to a substantial annual limitation under Section 382 and 383 of the Internal Revenue Code of 1986, and similar state provisions due to ownership change limitations that have occurred. These ownership changes will limit the amount of NOL and tax credit carry-forwards that can be utilized to offset future taxable income and tax, respectively.

We believe our existing cash and cash equivalents at December 31, 2011 will be sufficient to fund our operating requirements for at least the next 12 months.

Our cash requirements assumptions may prove to be wrong. Our future cash requirements will also depend on many factors, including:

progress in, and the costs of, future planned clinical trials and other research and development activities;

the scope, prioritization and number of our product development programs;

our obligations under our license agreements, pursuant to which we may be required to make future milestone payments upon the achievement of various milestones related to clinical, regulatory or commercial events;

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our ability to establish and maintain strategic collaborations, including licensing and other arrangements, and to complete acquisitions of additional product candidates;

the time and costs involved in obtaining regulatory approvals;

the costs of securing manufacturing arrangements for clinical or commercial production of our product candidates;

the costs associated with expanding our management, personnel, systems and facilities;

the costs associated with any litigation;

the costs associated with the operations or wind-down of any business it may acquire;

the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights; and

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the costs of establishing or contracting for sales and marketing capabilities and commercialization activities if we obtain regulatory approval to market our product candidates.

Based on our existing cash resources, we expect our research and development expenses to decline relative to 2011 as we completed the enrollment of our Phase 2 clinical trial of MN-221 for the treatment of acute exacerbations of asthma, as announced on March 21, 2012. If we are able to raise additional capital and/or enter into one or more strategic alliances, then we expect our research and development expenses to increase in connection with clinical trials primarily related to MN-221 for the treatment of acute exacerbations of asthma and COPD exacerbations, and any other development activities that we may initiate. In addition, our general and administrative expenses may increase in future periods as a result of several factors, including our research and development activities, our business development activities and any expansions in our infrastructure related to such activities. Our estimate of cash requirements for future operating expenses assumes that we do not commence a Phase 3 clinical trial for MN-221 and that we do not fund any further significant clinical development of MN-166 unless we are able to raise additional capital and/or enter into one or more strategic alliances. We do expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing drug products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

***If we fail to obtain the capital necessary to fund our operations, we will be unable to develop and commercialize our product candidates.***

We have consumed substantial amounts of capital since our inception. From our inception to December 31, 2011, we had an accumulated deficit of approximately \$285.3 million. Our cash and cash equivalents were approximately \$15.1 million at December 31, 2011.

Our business will continue to require us to incur substantial research and development expenses and we do not expect to be able to fund these expenses solely from upfront cash or milestones from collaborations or strategic alliances. As such we may be required to raise capital from one or more sources in the near term to continue our operations at or close to the levels currently conducted. We believe that without raising additional capital from accessible sources of financings, we will not otherwise have adequate funding to complete the development of MN-221 including pivotal clinical trials or the commercialization of any products we successfully develop. There is no guarantee that adequate funds will be available when needed from debt or equity financing, arrangements with partners, or from other sources, or on terms attractive to us. The inability to obtain sufficient additional funds when needed to fund our operations would require us to significantly delay, scale back, or eliminate some or all of our clinical or regulatory activities, further reduce general and administrative expenses and have a substantial negative effect on our results of operations and financial condition.

***We do not have any products that are approved for commercial sale and therefore do not expect to generate any revenues from product sales in the foreseeable future, if ever.***

To date, we have funded our operations primarily from sales of our securities and, to a lesser extent, debt financing. We have not received, and do not expect to receive for at least the next several years, if at all, any revenues from the commercialization of our product candidates. We anticipate that, prior to our commercialization of a product candidate, out-licensing upfront and milestone payments will be our primary source of revenue if we can enter into collaborations, strategic alliances or other agreements that would provide us with such revenues. To obtain revenues from sales of our product candidates, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing and marketing drugs with commercial potential. We may never succeed in these activities, and we may not generate sufficient revenues to continue our business operations or achieve and maintain profitability.

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***We are largely dependent on the success of our two prioritized product candidates, MN-221 and MN-166, and we cannot be certain that either of these product candidates will receive regulatory approval or be successfully commercialized.***

We currently have no products for sale, and we cannot guarantee that we will ever have any drug products approved for sale. The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA and comparable regulatory authorities in other countries. We are not permitted to market any of our product candidates in the U.S. until we submit and receive approval of a New Drug Application, or NDA, for a product candidate from the FDA or its foreign equivalent from a foreign regulatory authority. Obtaining FDA approval is a lengthy, expensive and uncertain process. We currently have two prioritized product candidates, MN-221 for the treatment of acute exacerbations of asthma and COPD exacerbations and MN-166, a combined ibudilast product development program covering MS and other CNS disorders, and the success of our business currently depends on their successful development and commercialization. Neither of these product candidates has completed the clinical development process; therefore, we have not submitted an NDA or foreign equivalent or received marketing approval for either of these two prioritized product candidates. In addition, we are not currently planning to fund any further significant clinical development of MN-166 until such time that we are able to secure a strategic collaboration to advance the combined development programs, which may delay or impede the process of completing clinical trials and seeking regulatory approval for this product candidate. We also cannot assure you that we will be able to secure such a strategic collaboration on attractive financial and other terms, or at all.

The clinical development programs for MN-221 and MN-166 may not lead to commercial products for a number of reasons, including our clinical trials' failure to demonstrate to the FDA's satisfaction that these product candidates are safe and effective or our failure to obtain necessary approvals from the FDA or similar foreign regulatory authorities for any reason. We may also fail to obtain the necessary approvals if we have inadequate financial or other resources to advance our product candidates through the clinical trial process or are unable to secure a strategic collaboration or partnership with a third party. Any failure or delay in completing clinical trials or obtaining regulatory approval for either MN-221 or MN-166 in a timely manner would have a material and adverse impact on our business and our stock price.

***We will depend on the joint venture company formed in China in 2011 to develop and commercialize MN-221 in China and there is no assurance that the joint venture will be able to be successful in doing so.***

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. We have invested \$650,000 for 30% interest in the joint venture company. 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 no assurances that the joint venture company will be successful in its efforts to conduct clinical trials necessary to gain regulatory approval in China, will be able to successfully manufacture drug candidates for the Chinese market or will receive the future funding it will require to conduct operations. 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 or that we will someday recover our investment in the joint venture company.

***We may not realize all of the anticipated benefits of the combined clinical development programs based on ibudilast.***

We may not be able to successfully secure a strategic collaboration to advance the combined ibudilast development programs. Following completion of the Phase 2 clinical trial of MN-166 for the treatment of MS in the second quarter of 2008 and the acquisition of Avigen in December 2009, we have not undertaken, nor do we plan to undertake, any further significant clinical development of MN-166 until such time that we secure a strategic collaboration to advance the combined clinical development of MN-166 ibudilast-based development program. We cannot assure you that we will be able to secure such a strategic collaboration or otherwise further advance, or recognize value from, a combined MN-166 clinical development program.





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*In order to commercialize a therapeutic drug successfully, a product candidate must receive regulatory approval after the successful completion of clinical trials, which are long, complex and costly, have a high risk of failure and can be delayed or terminated at any time.*

Our product candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. The process of obtaining FDA and other regulatory approvals is costly, time-consuming, uncertain and subject to unanticipated delays. To receive regulatory approval for the commercial sale of any of our product candidates, we must conduct, at our own expense, adequate and well-controlled clinical trials in human patients to demonstrate the efficacy and safety of the product candidate. Clinical testing is expensive, takes many years and has an uncertain outcome. To date, we have obtained regulatory authorization to conduct clinical trials for eight of our product development programs. Investigational New Drug Applications, or INDs, were approved by the FDA and are active for seven of our product candidates. We also have obtained Clinical Trial Authorizations, or CTAs, for the ongoing Phase 2 clinical trial for MN-221 in Canada, Australia and New Zealand. Through the acquisition of Avigen, we have assumed responsibility for clinical trials including one active IND for neuropathic pain and cross-reference and drug product support of the NIDA-funded opioid withdrawal investigator-initiated IND with Columbia University drug addiction clinical researchers. In the third quarter of 2010, the FDA approved a NIDA-funded investigator-initiated IND with University of California Los Angeles to proceed with an initial trial of our neurological drug candidate, ibudilast (MN-166), as a potential new pharmacotherapy for methamphetamine addiction. The study will be led by established clinical research investigators in the treatment of drug addiction.

It may take years to complete the clinical development necessary to commercialize a drug, and delays or failure can occur at any stage, which may result in our inability to market and sell any products derived from any of our product candidates that are ultimately approved by the FDA or foreign regulatory authorities. Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and/or non-clinical testing. For example, in October 2007, we announced that our Phase 2 clinical trial of MN-305 for the treatment of insomnia failed to achieve statistical significance in its primary endpoint, and, as a result, we terminated development of MN-305 for the treatment of insomnia. Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization. Interim results of clinical trials do not necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials even after obtaining promising results in earlier clinical trials. In addition, any delays in completing clinical trials or the rejection of data from a clinical trial by a regulatory authority will result in increased development costs and could have a material adverse effect on the development of the impacted product candidate.

In connection with the conduct of clinical trials for each of our product candidates, we face many risks, including the risks that:

the product candidate may not prove to be effective in treating the targeted indication;

clinical trial participants and/or patients may experience serious adverse events or other undesirable drug-related side effects;

the results may not confirm the positive results of earlier trials;

the FDA or other regulatory authorities may not agree with our proposed development plans or accept the results of completed clinical trials; and

our planned clinical trials and the data collected from such clinical trials may be deemed by the FDA or other regulatory authorities not to be sufficient, which would require additional development for the product candidate before it can be evaluated in late stage clinical trials or before the FDA will consider an application for marketing approval.



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If we do not complete clinical development of our product candidates successfully, we will be unable to obtain regulatory approval to market products and generate revenues from such product candidates. We may also fail to obtain the necessary regulatory approvals if we have inadequate financial or other resources to advance our product candidates through the clinical trial process. In addition, even if we believe that the preclinical and clinical data are sufficient to support regulatory approval for a product candidate, the FDA and foreign regulatory authorities may not ultimately approve such product candidate for commercial sale in any jurisdiction, which would limit our ability to generate revenues and adversely affect our business. In addition, even if our product candidates receive regulatory approval, they remain subject to ongoing FDA regulations, including obligations to conduct additional clinical trials, changes to the product label, new or revised regulatory requirements for manufacturing practices, written advisements to physicians, and/or a product recall or withdrawal.

*We are subject to stringent regulation of our product candidates, which could delay the development and commercialization of our product candidates.*

We, our third-party manufacturers, service providers, suppliers and partners, and our product candidates are subject to stringent regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. None of our product candidates can be marketed in the U.S. until it has been approved by the FDA. None of our product candidates has been approved by the FDA to date, and we may never receive FDA approval for any of our product candidates. Obtaining FDA approval for a product takes many years of clinical development and requires substantial resources. Additionally, changes in regulatory requirements and guidance may occur or new information regarding the product candidate or the target indication may emerge, and we may need to perform additional, unanticipated non-clinical or clinical testing of our product candidates or amend clinical trial protocols to reflect these changes. Any additional unanticipated testing would add costs and could delay or result in the denial of regulatory approval for a product candidate. These regulatory requirements may limit the size of the market for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could substantially reduce or negate our ability to generate revenues from the particular product candidate.

In addition, both before and after regulatory approval, we, our partners and our product candidates are subject to numerous FDA requirements, including requirements related to testing, manufacturing, quality control, labeling, advertising, promotion, distribution and export. The FDA's requirements may change and additional government regulations may be promulgated that could affect us, our partners and our product candidates. Given the number of recent high profile adverse safety events with certain drug products, the FDA may require, as a condition of approval, costly risk management programs, which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, preapproval of promotional materials and restrictions on direct-to-consumer advertising. Furthermore, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad.

In order to market any of our products outside of the U.S., we and our strategic partners and licensees must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods beyond the requirements of the FDA and the time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S. Regulatory approval in one country, including FDA approval in the U.S., does not ensure regulatory approval in another. In addition, a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. A product candidate may not be approved for all indications that we request, which would limit the uses of our product and adversely impact our potential royalties and product sales, and any approval that we receive may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

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If we fail to comply with applicable regulatory requirements in the U.S. or other countries, we may be subject to regulatory and other consequences, including fines and other civil penalties, delays in approving or failure to approve a product, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, interruption of manufacturing or clinical trials, injunctions and criminal prosecution, any of which would harm our business.

*Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.*

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies, including additional research and development and clinical trials. Any of these restrictions or requirements could adversely affect our potential product revenues. For example, the label ultimately approved for MN-221 or MN-166, our other product candidates or any other product candidates that we may in-license or acquire, if any, may include a restriction on the terms of its use, or it may not include one or more of our intended indications.

Our product candidates will also be subject to ongoing FDA requirements for the labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information on the drug. In addition, approved products, manufacturers and manufacturers' facilities are subject to continual review and periodic inspections. If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates fail to comply with applicable regulatory requirements, such as commercial good manufacturing practices, or cGMPs, a regulatory agency may:

issue warning letters or untitled letters;

require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;

impose other civil or criminal penalties;

suspend regulatory approval;

suspend any ongoing clinical trials;

refuse to approve pending applications or supplements to approved applications filed by us;

impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products or require a product recall.

*If we fail to obtain and maintain approval from regulatory authorities in international markets for any of our current or future product candidates for which we have rights in international markets, our market opportunities will be limited and our business will be adversely impacted.*

Sales of our product candidates outside of the U.S. will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of our product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the U.S., including additional preclinical studies or clinical trials. In many countries outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products is also subject to approval. Obtaining foreign regulatory approvals and

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compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others.

*The FDA may not ultimately approve our proposed trade names for our product candidates.*

Any trade names that we intend to use for our product candidates must be approved by the FDA irrespective of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or PTO. The FDA conducts a rigorous review of proposed product names and may reject a proposed product name for a variety of reasons, including if it believes that the name inappropriately implies medical claims or if it poses the potential for confusion with other product names. In addition, if the FDA determines that the trade names of other product candidates that are approved prior to the approval of our product candidates may present a risk of confusion with any of our proposed trade names, the FDA may not ultimately approve those proposed trade names. If the FDA does not approve any of our proposed product names prior to their applicable NDA approval dates, we may be required to launch commercial sales of such products without brand names, and our efforts to build successful brand identities for, and commercialize, such products may consequently be adversely impacted.

*Any product candidate that we develop may cause undesirable side effects or have other properties that could delay or prevent regulatory approval or commercialization.*

Undesirable side effects caused by any product candidate that we develop could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, or cause us to evaluate the future of our development programs. In addition, the FDA or other regulatory authorities may require, or we may undertake, additional clinical trials to support the safety profile of our product candidates.

In addition, if any product candidate that we may develop that receives marketing approval and we or others later identify undesirable side effects caused by the product, or there is a perception that the product is associated with undesirable side effects:

regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

regulatory authorities may withdraw their approval of the product or place restrictions on the way it is prescribed; and

we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product or implement a risk evaluation and mitigation strategy.

If any of these events occurred with respect to our product candidates, our ability to generate significant revenues from the sale of these products would be significantly harmed.

*Delays in the commencement or completion of clinical trials, or suspension or termination of our clinical trials, could result in increased costs to us and delay or limit our ability to obtain regulatory approval for our product candidates.*

If we experience delays in the commencement or completion of our clinical trials, we could incur significantly higher product development costs and our ability to obtain regulatory approvals for our product candidates could be delayed or limited. The commencement and completion of clinical trials requires us to identify and maintain a sufficient number of study sites and enroll a sufficient number of patients at such sites. We do not know whether enrollment in our future clinical trials for our product candidates will be completed on

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time, or whether our additional planned and ongoing clinical trials for our product candidates will be completed on schedule, if at all.

The commencement and completion of clinical trials can be delayed for a variety of other reasons, including delays in:

obtaining regulatory approval to commence or amend a clinical trial;

reaching agreements on acceptable terms with prospective clinical research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

recruiting and enrolling patients to participate in clinical trials;

retaining patients who have initiated a clinical trial but who may be prone to withdraw due to the treatment protocol, lack of efficacy, personal issues or side effects from the therapy or who are lost to further follow-up;

manufacturing sufficient quantities of a product candidate; and

IRB approval or approval from foreign counterparts to conduct or amend a clinical trial at a prospective site.

In addition, a clinical trial may be delayed, suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including:

ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results, which may result in the imposition of a clinical hold on the IND for any clinical trial, as well as the inability to resolve any outstanding concerns with the FDA so that a clinical hold already placed on the IND may be lifted and the clinical trial may begin;

inspections of our own clinical trial operations, the operations of our CROs or our clinical trial sites by the FDA or other regulatory authorities, which may result in the imposition of a clinical hold or potentially prevent us from using some of the data generated from our clinical trials to support requests for regulatory approval of our product candidates;

our failure or inability, or the failure or inability of our CROs, clinical trial site staff or other third party service providers involved in the clinical trial, to conduct clinical trials in accordance with regulatory requirements or our clinical protocols;

lower than anticipated enrollment or retention rates of patients in clinical trials;

new information suggesting unacceptable risk to subjects or unforeseen safety issues or any determination that a trial presents unacceptable health risks;



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insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials; and

lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties.

If we experience delays in the completion of our clinical trials for a product candidate, the commercial prospects for such product candidate may be harmed, we may incur increased costs for development of such product candidate and our ability to obtain regulatory approval for such product candidate could be delayed or limited. Many of the factors that cause or lead to delays in the commencement or completion of clinical trials

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may also ultimately lead to the denial of regulatory approval for a product candidate. In addition, any amendment to a clinical trial protocol may require us to resubmit our clinical trial protocols to IRBs or their foreign counterparts for reexamination, which may delay or otherwise impact the costs, timing or successful completion of a clinical trial.

*The loss of any rights to develop and market any of our product candidates could significantly harm our business.*

We license the rights to develop and market our product candidates. Currently, we have licensed rights relating to eight compounds for the development of ten product candidates.

We are obligated to develop and commercialize certain product candidates in accordance with mutually agreed upon terms and conditions. Our ability to satisfy some or all of the terms and conditions of our license agreements is dependent on numerous factors, including some factors that are outside of our control. Any of our license agreements may be terminated if we breach our obligations under the agreement materially and fail to cure any such breach within a specified period of time.

If any of our license agreements is terminated, we would have no further rights to develop and commercialize the product candidate that is the subject of the license. The termination of the license agreements related to either of our two prioritized product candidates would significantly and adversely affect our business. The termination of any of the remainder of our license agreements could materially and adversely affect our business.

*If our competitors develop and market products that are more effective than our product candidates, they may reduce or eliminate our commercial opportunities.*

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, in the U.S. and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our product development programs. We cannot assure you that developments by others will not render our product candidates obsolete or noncompetitive. Many of our competitors have products that have been approved or are in advanced development and may succeed in developing drugs that are more effective, safer, more affordable or more easily administered than ours, or that achieve patent protection or commercialization sooner than our products. Our competitors may also develop alternative therapies that could further limit the market for any products that we are able to obtain approval for, if at all. In addition, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical industry at a rapid pace. These developments may render our product candidates obsolete or noncompetitive.

In many of our target disease areas, potential competitors are working to develop new compounds with different mechanisms of action and attractive efficacy and safety profiles. Many of our competitors have substantially greater financial, research and development resources, including personnel and technology, clinical trial experience, manufacturing, sales and marketing capabilities and production facilities than we do. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies.

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Our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective and less costly than ours and may also be more successful than us in manufacturing and marketing their products. We also expect to face

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similar competition in our efforts to identify appropriate collaborators or partners to help develop or commercialize our product candidates.

*We will depend on strategic collaborations with third parties to develop and commercialize selected product candidates and will not have control over a number of key elements relating to the development and commercialization of these product candidates if we are able to achieve such third-party arrangements.*

A key aspect of our strategy is to seek collaborations with partners, such as large pharmaceutical companies, that are willing to conduct later-stage clinical trials and further develop and commercialize selected product candidates. Following completion of the Phase 2 clinical trial for MN-166 for the treatment of MS in the second quarter of 2008 and the acquisition of Avigen in December 2009, we do not plan to undertake any further significant clinical development activities for any of our product candidates other than MN-221 for the treatment of acute exacerbations of asthma and COPD exacerbations, other than those activities deemed necessary to maximize each product candidate's value, until such time that we are successful in entering into a partnership or collaboration for further development of such product candidates. To date, we have not entered into any such collaborative arrangements, and we may not be able to enter into any collaborations or otherwise monetize these product candidates on acceptable terms, if at all.

By entering into a strategic collaboration with a partner, we may rely on the partner for financial resources and for development, regulatory and commercialization expertise. Even if we are successful in entering into a strategic collaboration for one of our product candidates, our partner may fail to develop or effectively commercialize the product candidate because such partner:

does not have sufficient resources or decides not to devote the necessary resources due to internal constraints such as limited cash or human resources;

decides to pursue a competitive potential product developed outside of the collaboration;

cannot obtain the necessary regulatory approvals;

determines that the market opportunity is not attractive; or

cannot manufacture the necessary materials in sufficient quantities from multiple sources or at a reasonable cost.

We also face competition in our search for partners from other biotechnology and pharmaceutical companies worldwide, many of whom are larger and able to offer more attractive deals in terms of financial commitments, contribution of human resources, or development, manufacturing, regulatory or commercial expertise and support.

If we are not successful in attracting partners and entering into collaborations on acceptable terms for these product candidates or otherwise monetizing these product candidates, we may not be able to complete development of or obtain regulatory approval for such product candidates. In such event, our ability to generate revenues from such products and achieve or sustain profitability would be significantly hindered.

*The terms under which we raise additional capital or debt financing may harm our business and may significantly dilute stockholders ownership interests.*

If we raise additional funds through collaborations or licensing arrangements with third parties, we may need to relinquish some rights to our product candidates, including commercialization rights, which may hinder our ability to generate revenues and achieve or sustain profitability. If we raise additional funds by issuing equity securities, including as part of a debt financing, stockholders may experience substantial dilution. Debt financing, if available, may involve significant cash payment obligations and restrictive covenants and other financial terms

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that may impede our ability to operate our business. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders.

*We rely on third parties to conduct our clinical trials, and we may incur additional development costs, experience delays in the commencement and completion of clinical trials, and be unable to obtain regulatory approval for or commercialize our product candidates on our anticipated timeline if these third parties do not successfully carry out their contractual duties or meet expected deadlines.*

We rely extensively on CROs, medical institutions, clinical investigators, contract laboratories and other service providers to perform important functions related to the conduct of our clinical trials, the collection and analysis of data and the preparation of regulatory submissions. Although we design and manage our current clinical trials to ensure that each clinical trial is conducted in accordance with its investigational plan and protocol, we do not have the ability to conduct all aspects of our clinical trials directly for our product candidates.

The FDA requires us and our CROs to comply with regulations and standards, commonly referred to as good clinical practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. Our reliance on CROs does not relieve us of these responsibilities and requirements. The CROs, medical institutions, clinical investigators, contract laboratories and other service providers that we employ in the conduct of our clinical trials are not our employees, and we cannot control the amount or timing of resources that they devote to our product development programs. If any of these third parties fails to devote sufficient care, time and resources to our product development programs, if its performance is substandard, or if any third party is inspected by the FDA and found not to be in compliance with GCPs, it will delay the completion of the clinical trial in which they are involved and the progress of the affected development program. The CROs with which we contract for execution of our clinical trials play a significant role in the conduct of the clinical trials and the subsequent collection and analysis of data. Any failure of the CROs to meet their obligations could adversely affect clinical development of our product candidates. Moreover, the CROs, clinical investigators and other service providers may have relationships with other commercial entities, some of which may have competitive products under development or currently marketed, and our competitive position could be harmed if they assist our competitors. If any of these third parties does not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for our product candidates. In addition, while we believe that there are numerous alternative sources to provide these services, we might not be able to enter into replacement arrangements without delays or additional expenditures if we were to seek such alternative sources.

*We rely on third-party manufacturers to produce our product candidates, which may result in delays in our clinical trials and the commercialization of products, as well as increased costs.*

We have no manufacturing facilities, and we do not intend to develop facilities for the manufacture of our product candidates for clinical trials or commercial purposes in the foreseeable future. We contract with third-party manufacturers to produce, in collaboration with us, sufficient quantities of our product candidates for clinical trials, and we plan to contract with third-party manufacturers to produce sufficient quantities of any product candidates approved by the FDA or other regulatory authorities for commercial sale. While we believe that there are competitive sources available to manufacture our product candidates, we may not be able to enter into arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty.

Reliance on third-party manufacturers limits our ability to control certain aspects of the manufacturing process and therefore exposes us to a variety of significant risks, including risks related to our ability to commercialize any products approved by regulatory authorities or conduct clinical trials, reliance on such third



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parties for regulatory compliance and quality assurance, and the refusal or inability of a third-party manufacturer to supply our requirements on a long-term basis. In addition, manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel and compliance with federal, state and foreign regulations. Also, our manufacturers may not perform as agreed. If our manufacturers were to encounter any of these difficulties, our ability to timely produce our product candidates for clinical trials and commercial sale may be interrupted, which could result in delayed clinical trials or receipt of regulatory approval and lost or delayed revenues.

We have entered into an agreement with Hospira Worldwide, Inc. for the development and supply of finished product of MN-221 for the treatment of acute exacerbations of asthma and COPD that we intend to use in clinical trials and the commercial market if MN-221 receives regulatory approval. We do not have agreements established regarding commercial supply of finished product of MN-221 in standard vials or for the active pharmaceutical ingredient, or API, or finished product for any of our product candidates. Pursuant to our license agreement with Kissei Pharmaceutical Co., Ltd., we will negotiate with them a commercial supply agreement on commercially reasonable terms, in order to manufacture the API for MN-221 on a commercial scale if MN-221 is approved by the FDA or other regulatory authorities for commercial sale. We will also need to successfully negotiate a supply agreement with a third-party manufacturer on commercially reasonable terms in order to manufacture the finished product of MN-221 in standard vials. We may not be able to establish or maintain any commercial manufacturing and supply arrangements on commercially reasonable terms that we require for purposes of commercializing a product. Any failure by us to secure or maintain any such required commercial supply agreements could result in interruption of supply and lost or delayed revenues, which would adversely affect our business. Any problems or delays we experience in preparing for commercial-scale manufacturing of a product candidate may result in a delay in FDA or other regulatory approval of the product candidate or may impair our ability to manufacture commercial quantities, which would adversely affect our business. For example, our manufacturers will need to produce specific batches of a product candidate to demonstrate acceptable stability under various conditions and for commercially viable lengths of time. We and our third-party manufacturers will need to demonstrate to the FDA and other regulatory authorities this acceptable stability data for the product candidate, as well as validate methods and manufacturing processes, in order to receive regulatory approval to commercialize such product candidate.

Our manufacturers are obligated to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs and, in some cases, International Convention on Harmonization, or ICH, standards. A failure of any of our third-party manufacturers to establish and follow cGMPs and/or ICH standards and to document their adherence to such practices may lead to significant delays in our ability to timely conduct and complete clinical trials, obtain regulatory approval of product candidates or launch of our products into the market. In addition, changing third-party manufacturers is difficult. For example, a change in third-party manufacturer for a particular product candidate requires re-validation of the manufacturing processes and procedures in accordance with cGMPs, which may be costly and time-consuming and, in some cases, our manufacturers may not provide us with adequate assistance to transfer the manufacturing processes and procedures for our product candidates to new manufacturers or may possess intellectual property rights covering parts of these processes or procedures for which we may need to obtain a license. Failure by our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of regulatory approvals, seizures or recalls of products, operating restrictions and criminal prosecutions.

***We may not be able to manufacture our product candidates in commercial quantities, which would prevent us from commercializing our product candidates.***

To date, our product candidates have been manufactured in small quantities for preclinical studies and clinical trials. If any of our product candidates is approved by the FDA or comparable regulatory authorities in



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other countries for commercial sale, we will need to manufacture such product candidate in larger quantities. We may not be able to increase successfully the manufacturing capacity for any of our product candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we are unable to increase successfully the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply. Our product candidates require precise, high quality manufacturing. Our failure to achieve and maintain these high manufacturing standards in collaboration with our third-party manufacturers, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could harm our business, financial condition and results of operations.

*Materials necessary to manufacture our product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our product candidates.*

We rely on the third-party manufacturers of our product candidates to purchase from third-party suppliers the materials necessary to produce the API and product candidates for our clinical trials, and we will rely on such manufacturers to purchase such materials to produce the API and finished product for any commercial distribution of our products if we obtain marketing approval. Suppliers may not sell these materials to our manufacturers at the time they need them in order to meet our required delivery schedule or on commercially reasonable terms, if at all. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Moreover, we currently do not have any agreements for the production of these materials. If our manufacturers are unable to obtain these materials for our clinical trials, testing of the affected product candidate would be delayed, which may significantly impact our ability to develop the product candidate. If we or our manufacturers are unable to purchase these materials after regulatory approval has been obtained for one of our products, the commercial launch of such product would be delayed or there would be a shortage in supply of such product, which would harm our ability to generate revenues from such product and achieve or sustain profitability.

*Our product candidates, if approved for sale, may not gain acceptance among physicians, patients and the medical community, thereby limiting our potential to generate revenues.*

If one of our product candidates is approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product by physicians, healthcare professionals and third-party payers and our profitability and growth will depend on a number of factors, including:

demonstration of efficacy;

changes in the standard of care for the targeted indication;

relative convenience and ease of administration;

the prevalence and severity of any adverse side effects;

availability, cost and potential advantages of alternative treatments, including less expensive generic drugs;

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pricing and cost effectiveness, which may be subject to regulatory control;

effectiveness of our or any of our partners' sales and marketing strategies;

the product labeling or product insert required by the FDA or regulatory authority in other countries; and

the availability of adequate third-party insurance coverage or reimbursement.

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If any product candidate that we develop does not provide a treatment regimen that is as beneficial as, or is perceived as being as beneficial as, the current standard of care or otherwise does not provide patient benefit, that product candidate, if approved for commercial sale by the FDA or other regulatory authorities, likely will not achieve market acceptance. Our ability to effectively promote and sell any approved products will also depend on pricing and cost-effectiveness, including our ability to produce a product at a competitive price and our ability to obtain sufficient third-party coverage or reimbursement. If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, patients and third-party payors, our ability to generate revenues from that product would be substantially reduced. In addition, our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

*If our products are not accepted by the market or if users of our products are unable to obtain adequate coverage of and reimbursement for our products from government and other third-party payors, our revenues and profitability will suffer.*

Our ability to commercialize our products successfully will depend in significant part on pricing and cost effectiveness, including our ability to produce a product at a competitive price and our ability to obtain appropriate coverage of and reimbursement for our products and related treatments from governmental authorities, private health insurers and other organizations, such as health maintenance organizations, or HMOs. Third-party payors are increasingly challenging the prices charged for medical products and services. We cannot provide any assurances that third-party payors will consider our products cost-effective or provide coverage of and reimbursement for our products, in whole or in part.

Uncertainty exists as to the coverage and reimbursement status of newly approved medical products and services and newly approved indications for existing products. Third-party payors may conclude that our products are less safe, less clinically effective or less cost-effective than existing products, and third-party payors may not approve our products for coverage and reimbursement. If we are unable to obtain adequate coverage of and reimbursement for our products from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them. Such reduction or limitation in the use of our products could cause our sales to suffer. Even if third-party payors make reimbursement available, payment levels may not be sufficient to make the sale of our products profitable.

Market acceptance and sales of our current or future product candidates will depend in large part on global reimbursement policies and may be affected by future healthcare reform measures, both in the U.S. and other key international markets. For example, continuing health care reform in the U.S. will control or significantly influence the purchase of medical services and products, and may result in inadequate coverage of and reimbursement for our products. Many third-party payors are pursuing various ways to reduce pharmaceutical costs, including the use of formularies. The market for our products depends on access to such formularies, which are lists of medications for which third-party payors provide reimbursement. These formularies are increasingly restricted, and pharmaceutical companies face significant competition in their efforts to place their products on formularies. This increased competition has led to a downward pricing pressure in the industry. The cost containment measures that third-party payors, including government payors, are instituting could have a material adverse effect on our ability to operate profitably.

Internationally, the success of our product candidates, if approved, will depend largely on obtaining and maintaining government reimbursement, because in many European countries patients are unlikely to use prescription drugs that are not reimbursed by their governments. Negotiating prices with governmental authorities can delay commercialization by 12 months or more. Reimbursement policies may adversely affect our ability to sell our product candidates, if approved, on a profitable basis. In many international markets, governments control the prices of prescription pharmaceuticals, including through the implementation of reference pricing, price cuts, rebates, revenue-related taxes and profit control, and expect prices of prescription pharmaceuticals to decline over the life of the product or as volumes increase. Recently, many countries in the

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European Union have increased the amount of discounts required on pharmaceutical products, which may impact the reimbursement rates and timing to launch product candidates. Such pricing practices may affect our ability to achieve profitability or expected rates of growth in revenue or results of operations, which in turn could adversely affect our business, financial condition and results of operations.

*If we fail to identify and license or acquire other product candidates, we will not be able to expand our business over the long term.*

Because we do not have internal discovery capabilities, our business over the long term is substantially dependent on our ability to license or acquire product candidates and further develop them for commercialization. The success of this strategy depends upon our ability to identify, select and acquire the right product candidates. We have limited experience identifying, negotiating and implementing economically viable product candidate acquisitions or licenses, which is a lengthy and complex process. Also, the market for licensing and acquiring product candidates is intensely competitive, and many of our competitors have greater resources than we do. We may not have the requisite capital resources to consummate product candidate acquisitions or licenses that we identify to fulfill our strategy.

Moreover, product candidate acquisitions that we do complete involve numerous risks, including:

difficulties in integrating the development program for the acquired product candidate into our existing operations;

diversion of financial and management resources from existing operations;

risks of entering new markets or technologies and of receiving regulatory approval;

inability to generate sufficient revenues to offset acquisition costs; and

delays that may result from our having to perform unanticipated preclinical trials or other tests on the product candidate.

If we are not successful in identifying and licensing or acquiring other product candidates over the long term, we will not be able to grow our revenues with sales from new products beyond those revenues, if any, from any approved products derived from our existing product candidates, and we may fail to achieve or sustain profitability.

*We are dependent on our management team, Yuichi Iwaki, M.D., Ph.D., and experienced scientific staff, and if we are unable to retain, motivate and attract key personnel, our product development programs may be delayed and we may be unable to develop successfully or commercialize our product candidates.*

We are dependent upon the continued services of our executive officers and other key personnel, particularly Yuichi Iwaki, M.D., Ph.D., a founder of the company and our President and Chief Executive Officer, who has been instrumental in our ability to in-license product candidates from Japanese pharmaceutical companies and secure financing from Japanese institutions. The relationships that certain of our key managers have cultivated with pharmaceutical companies from whom we license product candidates and to whom we expect to out-license product candidates make us particularly dependent upon their continued services with us, whether through employment, service on our board of directors

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or a consulting agreement. We are also substantially dependent on the continued services of clinical development personnel because of the highly technical nature of our product development programs. We are not presently aware of any plans of our executive officers or key personnel to retire or leave employment with the company. Each of our executive officers is party to an employment agreement that continues in effect until the earliest of termination of employment by (i) consent of the parties, (ii) cause or other material breach of the agreement, (iii) death or permanent disability or (iv) three months' written notice. Following termination of employment, these individuals may engage in other businesses that may compete with us.

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If we acquire or license new product candidates, our success will depend on our ability to attract, retain and motivate highly qualified management and scientific personnel to manage the development of these new product candidates. In particular, our product development programs depend on our ability to attract and retain highly experienced clinical development and regulatory personnel. However, we face competition for experienced scientists and other technical and professional personnel from numerous companies and academic and other research institutions. Competition for qualified personnel is particularly intense in the San Diego, California area, where our corporate headquarters is located. Our short operating history and the uncertainties attendant to being a development stage biopharmaceutical company could impair our ability to attract and retain personnel and impede the achievement of our development and commercialization objectives. In addition, we have scientific and clinical advisors who assist us in our product development and clinical strategies. These third parties are not our employees and may have commitments to, or contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with our product candidates.

Although we have employment agreements with key members of management, each of our employees, subject to applicable notice requirements, may terminate his or her employment at any time. We do not carry key person insurance covering members of senior management. If we lose any of our key management personnel, we may not be able to find suitable replacements, which would adversely affect our business.

***If we are unable to establish sales, marketing and distribution capabilities, whether independently or with third parties, we will be unable to successfully commercialize our product candidates.***

To date, we have not sold, marketed or distributed any pharmaceutical products. If we are successful in obtaining regulatory approvals for any of our product candidates or acquiring other approved products, we will need to establish sales, marketing and distribution capabilities on our own or with partners in order to commercialize an approved product. The acquisition or development of an effective sales and marketing infrastructure will require a significant amount of our financial resources and time and could negatively impact our commercialization efforts, including delay of a product launch. We may be unable to establish and manage a sufficient or effective sales force in a timely or cost-effective manner, if at all, and any sales force we do establish may not be capable of generating demand for our products, therefore hindering our ability to generate revenues and achieve or sustain profitability. In addition, if we are unable to develop internal sales capabilities, we will need to contract with third parties or establish a partnership to market and sell the product. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate any product revenues, may generate increased expenses and may never become profitable. In addition, although we intend to establish strategic collaborations to market any products approved for sale by regulatory authorities outside of the U.S., we may be required to market our product candidates outside of the U.S. directly if we are unable to establish such collaborations. In that event, we may need to build a corresponding international sales and marketing capability with technical expertise and with supporting distribution capabilities.

***Health care reform measures could adversely affect our business.***

The business and financial condition of pharmaceutical and biotechnology companies are affected by the efforts of governmental and third-party payors to contain or reduce the costs of health care. In the U.S. and in foreign jurisdictions, there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the health care system. For example, in some countries, pricing of prescription drugs is subject to government control, and we expect proposals to implement similar controls in the U.S. to continue. Another example of proposed reform that could affect our business is drug reimportation into the U.S. Moreover, the pendency or approval of such proposals could result in a decrease in our stock price or our ability to raise capital or to obtain strategic partnerships or licenses. More recently, the President signed into law the Patient Protection and Affordable Care Act, which imposes numerous provisions over a four-year period.



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We have begun to assess the impact of this Act, but, at this early stage the likely impact cannot be ascertained with any degree of certainty.

*We may be sued for product liability, which could result in substantial liabilities that exceed our available resources and damage our reputation.*

The development and commercialization of drug products entails significant product liability risks. Product liability claims may arise from use of any of our product candidates in clinical trials and the commercial sale of any approved products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

withdrawal of clinical trial participants;

termination of clinical trial sites or entire clinical trial programs;

decreased demand for our product candidates;

impairment of our business reputation;

costs of related litigation;

substantial monetary awards to patients or other claimants;

loss of revenues; and

the inability to commercialize our product candidates.

We currently have insurance that covers our clinical trials. We believe our current insurance coverage is reasonably adequate at this time; however, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for all expenses or losses we may suffer. In addition, we will need to increase and expand this coverage as we commence additional clinical trials, as well as larger scale clinical trials, and in the event that any of our product candidates is approved for commercial sale. This insurance may be prohibitively expensive or may not fully cover our potential liabilities. In addition, our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the regulatory approval or commercialization of products that we or one of our collaborators develop. Successful product liability claims could have a material adverse effect on our business and results of operations. Liability from such claims could exceed our total assets if we do not prevail in any lawsuit brought by a third party alleging that an injury was caused by one of our product candidates.

*We may need to increase the size of our organization, and we may encounter difficulties managing our growth, which could adversely affect our results of operations.*



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We have 14 full-time employees as of the date of this report, following a reduction in force which took place in January 2011, wherein we down-sized the company to save costs. If we are successful in securing a strategic collaboration or raising additional capital, our management, personnel, systems and facilities currently in place may not be adequate to support the company's needs. For example, we may hire additional personnel in clinical development, regulatory affairs and business development to further strengthen our core competencies or choose to develop sales, marketing and distribution capabilities for certain of our product candidates. Our need to effectively manage our operations, growth and product development programs requires that we:

manage our clinical trials effectively;

manage our internal development efforts effectively while carrying out our contractual obligations to licensors and other third parties;

ensure that our consultants, CROs and other service providers successfully carry out their contractual obligations, provide high quality results and meet expected deadlines; and

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continue to improve our operational, financial and management controls, reporting systems and procedures.

We may be unable to successfully implement these tasks on a larger scale, which may impact our ability to timely achieve our development and commercialization goals, if at all.

*We expect that our results of operations will fluctuate, which may make it difficult to predict our future performance from period to period.*

Our quarterly operating results have fluctuated in the past and are likely to continue to do so in the future. Some of the factors that could cause our operating results to fluctuate from period to period include:

the status of development of our product candidates and, in particular, the advancement or termination of activities related to our product development programs and the timing of any milestone payments payable under our licensing agreements;

the execution of other collaboration, licensing and similar arrangements and the timing of payments we may make or receive under these arrangements;

variations in the level of expenses related to our product development programs;

the unpredictable effects of collaborations during these periods;

the timing of our satisfaction of applicable regulatory requirements, if at all;

the rate of expansion of our clinical development and other internal research and development efforts;

the costs of any litigation;

the effect of competing technologies and products and market developments; and

general and industry-specific economic conditions.

We believe that quarterly or yearly comparisons of our financial results are not necessarily meaningful and should not be relied upon as indications of our future performance.

*Our management has broad discretion over the use of our cash, and we may not use our cash effectively, which could adversely affect our results of operations.*

Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which may cause our stock price to decline.

*We will continue to incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.*

As a public company, we are required to comply with the Sarbanes-Oxley Act of 2002, as well as rules and regulations implemented by the SEC, The Nasdaq Stock Market, or Nasdaq, and Japanese securities laws, and incur significant legal, accounting and other expenses as a result. These rules impose various requirements on public companies, including requiring the establishment and maintenance of effective disclosure and financial controls and appropriate corporate governance practices. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and may make it more difficult and expensive for us to renew our director and officer liability insurance, and may result in imposition of reduced policy limits and coverage.

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The Sarbanes-Oxley Act requires that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Our listing obligations under the Nasdaq Market (formerly the Hercules Market until its closure in 2010) of the Osaka Securities Exchange, or OSE, also require that we comply either with Section 404 of the Sarbanes-Oxley Act or equivalent regulations in Japan and we elected to comply with Section 404. As a result, we are required to perform an evaluation of our internal control over financial reporting to allow management to report on the effectiveness of those controls, as required by Section 404. We are subject to attestation by our registered public accounting firm on our report regarding internal control over financial reporting for the year ended December 31, 2011 under Japanese securities laws. Our efforts to comply with Section 404 and related regulations have required, and continue to require, the commitment of significant financial and managerial resources. We cannot be certain that a material weakness will not be identified when we test the effectiveness of our controls in the future. If a material weakness is identified, we could be subject to sanctions or investigations by Nasdaq, the SEC, the OSE or other regulatory authorities, which would require additional financial and management resources, costly litigation or a loss of public confidence in our internal controls, which could have an adverse effect on the market price of our stock.

Additionally, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as say on pay and proxy access. To maintain high standards of corporate governance and public disclosure, we intend to invest all reasonably necessary resources to comply with such compliance programs and rules and all other evolving standards. These investments may result in increased general and administrative costs and a diversion of our management's time and attention from strategic revenue generating and cost management activities.

***Our business and operations would suffer in the event of system failures.***

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our drug development programs, including delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability and the further development of our product candidates may be delayed.

***A variety of risks associated with operating our business and marketing our products internationally could materially adversely affect our business.***

A significant amount of our business activity is outside of the United States. We face risks associated with our international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. We are subject to numerous risks associated with international business activities, including, but not limited to:

compliance with differing or unexpected regulatory requirements for our products;

difficulties in staffing and managing foreign operations;

in certain circumstances, including with respect to the commercialization of our product candidates in Europe, increased dependence on the commercialization efforts of our distributors or strategic partners;

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foreign government taxes, regulations and permit requirements;

U.S. and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;

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economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries;

fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues, and other obligations related to doing business in another country;

compliance with tax, employment, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;

workforce uncertainty in countries where labor unrest is more common than in the U.S.;

changes in diplomatic and trade relationships; and

challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the U.S.

These and other risks associated with our international operations may materially adversely affect our business, financial condition and results of operations.

## **Risks Related to Our Intellectual Property**

### ***Our ability to compete may decline if we do not adequately protect our proprietary rights.***

There is the risk that our patents (both those owned by us and those in-licensed) may not provide a competitive advantage, including the risk that our patents expire before we obtain regulatory and marketing approval for one or more of our product candidates, particularly our in-licensed patents. Also, our competitors may develop products similar to ours using methods and technologies that are beyond the scope of our intellectual property rights. Composition of matter patents on APIs may provide protection for pharmaceutical products without regard to formulation, method of use, or other type of limitation. We do not have compound patent protection for the API in our MN-166 and MN-001 product candidates, although we do have patent protection for a particular crystalline polymorph of MN-001 and we have composition of matter protection on ibudilast analogs. As a result, competitors that obtain the requisite regulatory approval will be able to offer products with the same API as found in our MN-166 and MN-001 product candidates so long as such competitors do not infringe any methods of use, methods of manufacture, formulation or, in the case of MN-001, specific polymorph patents that we hold or have exclusive rights to through our licensors. For example, we currently rely on method of use patents for MN-166.

It is our policy to consult with our licensors in the maintenance of granted patents we have licensed and in their pursuit of patent applications that we have licensed, but each of our licensors generally remains primarily responsible for or in control of the maintenance of the granted patents and prosecution of the applications. We have limited control, if any, over the amount or timing of resources that each licensor devotes on our behalf, and a licensor may not assign as great a priority to prosecution of these patent applications as we would if we were undertaking such prosecution ourselves. As a result of this lack of control and general uncertainties in the patent prosecution process, we cannot be sure that our licensed patents will be maintained and that any additional patents will ever mature from our licensed applications. Issued U.S. patents require the payment of maintenance fees to continue to be in force. We typically rely on our licensors to do this and their failure to do so could result in the forfeiture of patents not timely maintained. Many foreign patent offices also require the payment of periodic annuities to keep patents and patent applications in good standing. As we generally do not maintain control over the payment of annuities, we cannot be certain that our

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licensors will timely pay such annuities and that the granted patents and pending patent applications will not become abandoned. For example, certain annuities were not paid in a timely manner with respect to foreign patents licensed under MN-002 (the active metabolite of MN-001) and, as a result, our patent rights may be impaired in those territories. In addition, our licensors may have selected a limited amount of foreign patent protection, and therefore applications have not been filed in, and foreign patents may not have been perfected in, all commercially significant countries.

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The patent protection of our product candidates and technology involves complex legal and factual questions. Most of our license agreements give us a right, but not an obligation, to enforce our patent rights. To the extent it is necessary or advantageous for any of our licensors cooperation in the enforcement of our patent rights, we cannot control the amount or timing of resources our licensors devote on our behalf or the priority they place on enforcing our patent rights. We may not be able to protect our intellectual property rights against third party infringement, which may be difficult to detect, especially for infringement of patent claims for methods of manufacturing. Additionally, challenges may be made to the ownership of our intellectual property rights, our ability to enforce them or our underlying licenses, which in some cases have been made under foreign laws and may provide different protections than that of U.S. law.

We cannot be certain that any of the patents or patent applications owned by us or our licensors related to our product candidates and technology will provide adequate protection from competing products. Our success will depend, in part, on whether we or our licensors can:

obtain and maintain patents to protect our product candidates;

obtain and maintain any required or desirable licenses to use certain technologies of third parties, which may be protected by patents;

protect our trade secrets and know-how;

operate without infringing the intellectual property and proprietary rights of others;

enforce the issued patents under which we hold rights; and

develop additional proprietary technologies that are patentable.

The degree of future protection for our proprietary rights is uncertain. For example:

we or our licensor might not have been the first to make the inventions covered by each of our pending patent applications or issued patents;

we or our licensor might not have been the first to file patent applications for these inventions;

others may independently develop similar or alternative technologies or duplicate any of our technologies;

it is possible that none of our pending patent applications will result in issued patents;

any patents under which we hold rights may not provide us with a basis for maintaining market exclusivity for commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties as invalid, not infringed or unenforceable under U.S. or foreign laws; or



any of the issued patents under which we hold rights may not be valid or enforceable or may be circumvented successfully in light of the continuing evolution of domestic and foreign patent laws.

***Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.***

Because we operate in the highly technical field of research and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary trade secrets and unpatented know-how. However, trade secrets are difficult to protect, and we cannot be certain that others will not develop the same or similar technologies on their own. We have taken steps, including entering into confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors, to protect our trade secrets and unpatented know-how. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known

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to the party by us during the course of the party's relationship with us. We also typically obtain agreements from these parties which provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Further, we have limited control, if any, over the protection of trade secrets developed by our licensors. Enforcing a claim that a party illegally obtained and is using our trade secrets or know-how is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. may be less willing to protect trade secrets or know-how. The failure to obtain or maintain trade secret protection could adversely affect our competitive position.

*A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.*

There is significant litigation in our industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, their methods of use, manufacturing or other technologies or activities infringe the intellectual property rights of such third parties. There are many patents relating to chemical compounds and methods of use. If our compounds or their methods of use or manufacture are found to infringe any such patents, we may have to pay significant damages or seek licenses under such patents. We have not conducted comprehensive searches for unexpired patents issued to third parties relating to our product candidates. Consequently, no assurance can be given that unexpired, third-party patents containing claims covering our product candidates, their methods of use or manufacture do not exist. Moreover, because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, and because patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after filing, we cannot be certain that others have not filed patent applications that will mature into issued patents that relate to our current or future product candidates and which could have a material effect in developing and commercializing one or more of our product candidates. The owner of a patent that is arguably infringed can bring a civil action seeking to enjoin an accused infringer from importing, making, marketing, distributing, using or selling an infringing product. We may need to resort to litigation to enforce our intellectual property rights or to seek a declaratory judgment concerning the scope, validity or enforceability of third-party proprietary rights. Similarly, we may be subject to claims that we have inappropriately used or disclosed trade secrets or other proprietary information of third parties. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to:

payment of actual damages, royalties, lost profits, potential enhanced damages and attorneys' fees, if any infringement for which we are found liable is deemed willful, or a case against us is determined by a judge to be exceptional;

injunctive or other equitable relief that may effectively block our ability to further develop, commercialize and sell our products;

having to enter into license arrangements that may not be available on reasonable or commercially acceptable terms; or

significant cost and expense, as well as distraction of our management from our business.

As a result, we could lose our ability to develop and commercialize current or future product candidates.

*We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.*

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As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential

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competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

## **Risks Related to the Securities Markets and Investment in Our Common Stock**

*Our stock price may be volatile, and you may not be able to resell our shares at a profit or at all.*

Despite the listing of our common stock on the Nasdaq Global Market and the Jasdaq Market of the Osaka Securities Exchange in Japan, trading volume in our securities has been light and an active trading market may not develop for our common stock. In December 2011, our average trading volume was approximately 7,000 shares per day on the Nasdaq Global Market and approximately 10,000 shares per day on the Jasdaq Market.

The market prices for securities of biopharmaceutical and biotechnology companies, and early-stage drug discovery and development companies like us in particular, have historically been highly volatile and may continue to be highly volatile in the future. For example, since the date of our initial public offering in Japan on February 8, 2005 through December 31, 2011, our common stock has traded as high as approximately \$42.00 and as low as approximately \$1.40. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

the development status of our product candidates, including clinical trial results and determinations by regulatory authorities with respect to our product candidates, and particularly our prioritized product candidates;

the initiation, termination, or reduction in the scope of any collaboration arrangements or any disputes or developments regarding such collaborations;

FDA or foreign regulatory actions, including failure to receive regulatory approval for any of our product candidates;

announcements of technological innovations, new commercial products or other material events by us or our competitors;

disputes or other developments concerning our intellectual property rights;

market conditions in the pharmaceutical and biotechnology sectors;

actual and anticipated fluctuations in our quarterly or annual operating results;

price and volume fluctuations in the overall stock markets;

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any potential delisting of our securities;

changes in, or failure to meet, securities analysts' or investors' expectations of our financial performance;

additions or departures of key personnel;

discussions of our business, management, products, financial performance, prospects or stock price by the financial and scientific press and online investor communities;

litigation or public concern about the safety of our potential products;

public concern as to, and legislative action with respect to, the pricing and availability of prescription drugs or the safety of drugs and drug delivery techniques; or

regulatory developments in the U.S. and in foreign countries.

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Broad market and industry factors, as well as economic and political factors, also may materially adversely affect the market price of our common stock.

*We may become involved in securities class action litigation that could divert management's attention and harm our business.*

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biotechnology and biopharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

*Future sales of our common stock may cause our stock price to decline and may make it difficult to sell your shares.*

Sales of substantial amounts of our common stock, or the availability of such common stock for sale, could adversely affect the prevailing market prices for our common stock. If this occurs and continues, it could impair our ability to raise additional capital through the sale of securities should we desire to do so. In addition, it may be difficult, or even impossible, to find a buyer for shares of our common stock.

We have also registered all common stock that we may issue under our current employee benefits plans and upon exercise of warrants. As a result, these shares can be freely sold in the public market upon issuance, subject to the terms of the underlying agreements governing the grants and the restrictions of the securities laws. In addition, our directors and officers may in the future establish programmed selling plans under Rule 10b5-1 of the Exchange Act, for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

*Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us more complicated and the removal and replacement of our directors and management more difficult.*

Our restated certificate of incorporation and amended and restated bylaws contain provisions that may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock or adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. These provisions may also make it difficult for stockholders to remove and replace our board of directors and management. These provisions:

establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least a majority of our capital stock;

authorize the issuance of blank check preferred stock that could be issued by our board of directors in a discriminatory fashion designed to increase the number of outstanding shares and prevent or delay a takeover attempt;

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limit who may call a special meeting of stockholders;

establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings;

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prohibit our stockholders from making certain changes to our Restated Certificate of Incorporation or Amended and Restated Bylaws except with 66<sup>2</sup>/<sub>3</sub> percent stockholder approval; and

provide for a classified board of directors with staggered terms.

We also may be subject to provisions of the Delaware corporation law that, in general, prohibit any business combination with a beneficial owner of 15 percent or more of our common stock for three years unless the holder's acquisition of our stock was approved in advance by our board of directors. Although we believe these provisions collectively provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In any event, these provisions may delay or prevent a third party from acquiring us. Any such delay or prevention could cause the market price of our common stock to decline.

*We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.*

We have paid no cash dividends on any of our classes of capital stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

## **Item 1B. Unresolved Staff Comments**

Not applicable.

## **Item 2. Properties**

We lease approximately 5,089 square feet of office space at our headquarters in San Diego, California under a lease that expires in May 2012. On March 19, 2012, we entered into a sixth amendment of our lease agreement of our headquarters which extends the lease term through February, 2013. We have no laboratory, research or manufacturing facilities, and we currently do not plan to purchase or lease any such facilities, as such services are provided to us by third-party service providers. We believe that our current facilities are adequate for our needs for the immediate future and that, should it be needed, suitable additional space will be available to accommodate expansion of our operations on commercially reasonable terms. In addition to our headquarters, we also lease approximately 1,726 square feet of office space in Tokyo, Japan under a lease that expires in May 2013.

## **Item 3. Legal Proceedings**

On March 3, 2011, we received a letter, in which certain allegations were made, from a former employee who had been terminated in January 2011 pursuant to our planned reduction-in-force. On July 8, 2011, the former employee filed a lawsuit in the Superior Court of the State of California, County of San Diego, asserting certain claims related to the Company's work environment and the employee's termination, and on



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December 12, 2011 the court granted our motion to compel arbitration. We have engaged legal counsel in this matter. Based on our current assessment, we do not expect its outcome to have a material adverse effect on our business, financial condition and results of operations.

We may become involved from time to time in various disputes and legal proceedings which arise in the ordinary course of business. Litigation and governmental investigations can be expensive and disruptive to normal business operations. While it is difficult to accurately predict the outcome of these matters, significant judgments or settlements in connection with legal proceedings could have a material adverse effect on our business, financial condition and results of operations.

### **Item 4. Mine Safety Disclosures**

Not applicable.

**Table of Contents****PART II****Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities****Market Information**

Our common stock is traded on the Jasdaq Market under the symbol 4875 and on the Nasdaq Global Market under the symbol MNOV. Our stock had been traded on the Hercules Market since February 8, 2005 (through the Hercules Market's closure in 2010) and now is currently traded on the Jasdaq Market and on the Nasdaq Global Market since December 7, 2006.

The following table sets forth the high and low sale prices per share of our common stock as reported on the Nasdaq Global Market.

	<b>Common Stock Price</b>	
	<b>High</b>	<b>Low</b>
<b>Fiscal year ended December 31, 2010</b>		
First quarter	\$ 9.00	\$ 6.09
Second quarter	\$ 7.51	\$ 4.75
Third quarter	\$ 6.40	\$ 4.44
Fourth quarter	\$ 5.95	\$ 4.51
<b>Fiscal year ended December 31, 2011</b>		
First quarter	\$ 5.90	\$ 2.56
Second quarter	\$ 2.72	\$ 1.94
Third quarter	\$ 3.08	\$ 1.88
Fourth quarter	\$ 2.44	\$ 1.60

**Holder of Common Stock**

As of the date of this filing there were approximately 7,000 holders of record of our common stock.

**Dividend Policy**

We have never declared or paid any cash dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future. We expect to retain our future earnings, if any, to fund the growth and development of our business.

**Use of Proceeds**

On March 23, 2011, we consummated a firm-commitment underwritten public offering of 2,750,000 units at a price to the public of \$3.00 per unit for gross proceeds of \$8.25 million. Each unit consists of one share of common stock, and a warrant to purchase one share of common stock. The shares of common stock and warrants are immediately separable and were issued separately. On March 24, 2011, the underwriter exercised 50,666 units of its 412,500 unit overallocation. The warrants are exercisable immediately upon issuance, have a five-year term and an exercise price of \$3.56 per share. The warrants are indexed to our stock and do not permit net-cash settlement. On March 29, 2011, we received net proceeds of approximately \$7.7 million, after underwriter discount and underwriter expenses and no warrants exercised. We are using and intend to continue to use the net proceeds to fund development work for MN-221 and for other research and development on MN-166. We may also use a portion of the net proceeds to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so.

**Table of Contents****Securities Authorized for Issuance Under Equity Compensation Plans**

Information regarding the securities authorized for issuance under our equity compensation plans can be found under Item 12 of this Annual Report on Form 10-K.

**Performance Graph**

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since February 8, 2005, which is the date our common stock first began trading on the Hercules Market of the Osaka Securities Exchange, to two indices: the Hercules Total Index and the Hercules Standard Index., through December 31, 2009. The graph assumes an initial investment of \$100 on February 8, 2005, and that all dividends were reinvested.

	<b>2/8/2005</b>	<b>12/30/2005</b>	<b>12/29/2006</b>	<b>12/28/2007</b>	<b>12/30/2008</b>	<b>12/30/2009</b>
MediciNova, Inc.	\$ 100	\$ 36	\$ 42	\$ 14	\$ 5	\$ 19
Hercules Total Index	\$ 100	\$ 153	\$ 73	\$ 48	\$ 20	\$ 23
Hercules Standard Index	\$ 100	\$ 162	\$ 86	\$ 59	\$ 25	\$ 26

\* No cash dividends have been declared or paid on our common stock. Stockholder returns over the indicated period should not be considered indicative of future stockholder returns.

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**Performance Graph**

Due to the closure of the Hercules Market of the Osaka Securities Exchange and the inability to retrieve our stock's performance from the Hercules Market in 2010, the following graph illustrates a comparison of the total cumulative stockholder return on our common stock since March 31, 2010, to the Jasdaq Market (total index). The graph assumes an initial investment of \$100 on March 31, 2010, and that all dividends were reinvested.

	3/31/2010	6/30/2010	9/30/2010	12/30/2010	3/31/2011	6/30/2011	9/30/2011	12/30/2011
MediciNova, Inc.	\$ 100	\$ 67	\$ 64	\$ 60	\$ 34	\$ 35	\$ 28	\$ 22
Jasdaq Total Index	\$ 100	\$ 96	\$ 90	\$ 98	\$ 96	\$ 98	\$ 92	\$ 90

\* No cash dividends have been declared or paid on our common stock. Stockholder returns over the indicated period should not be considered indicative of future stockholder returns.

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The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since December 7, 2006 which is the date our common stock first began trading on the Nasdaq Global Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of \$100 on December 7, 2006, and that all dividends were reinvested.

\* No cash dividends have been declared or paid on our common stock. Stockholder returns over the indicated period should not be considered indicative of future stockholder returns.

	<b>12/7/2006</b>	<b>12/31/2007</b>	<b>12/31/2008</b>	<b>12/31/2009</b>	<b>12/31/2010</b>	<b>12/30/2011</b>
MediciNova, Inc.	\$ 100	\$ 38	\$ 13	\$ 58	\$ 39	\$ 14
NASDAQ Biotechnologies Index	\$ 100	\$ 101	\$ 88	\$ 102	\$ 117	\$ 131
NASDAQ Composite Index	\$ 100	\$ 109	\$ 65	\$ 93	\$ 109	\$ 107

**Table of Contents****Item 6. Selected Financial Data.**

The selected financial data set forth below is derived from our audited consolidated financial statements and may not be indicative of future operating results. The following selected financial data should be read in conjunction with the Consolidated Financial Statements and notes thereto and Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. Amounts are in thousands, except per share amounts.

	Years ended December 31,					September 26, 2000 (inception) to December 31, 2011
	2011	2010	2009	2008	2007	
<b>Statements of Operations Data:</b>						
Revenues	\$	\$	\$	\$	\$	\$ 1,558
Operating expenses:						
Cost of revenues						1,258
Research and development	7,784	9,711	10,873	13,828	42,121	162,042
General and administrative	8,324	8,172	10,366	8,773	11,373	105,523
Total operating expenses	16,108	17,883	21,239	22,601	53,494	268,823
Operating loss	(16,108)	(17,883)	(21,239)	(22,601)	(53,494)	(267,265)
(Impairment charge)/gain, net on investment securities and ARS put		(785)	310	(1,260)		(1,735)
Other expense	(81)	(177)	(14)	(88)		(360)
Interest expense	(1,595)	(1,768)	(242)			(3,606)
Other income, net	62	439	823	2,038	4,611	19,121
Loss before income taxes	(17,722)	(20,174)	(20,362)	(21,911)	(48,883)	(253,845)
Income Taxes	(12)	(13)	(7)	(14)	(20)	(65)
Net loss	(17,734)	(20,187)	(20,369)	(21,925)	(48,903)	(253,910)
Accretion to redemption value of redeemable convertible preferred stock						(99)
Deemed dividend resulting from beneficial conversion on Series C redeemable convertible preferred stock						(31,264)
Net loss applicable to common stockholders	\$ (17,734)	\$ (20,187)	\$ (20,369)	\$ (21,925)	\$ (48,903)	\$ (285,273)
Basic and diluted net loss per share	\$ (1.20)	\$ (1.63)	\$ (1.68)	\$ (1.82)	\$ (4.16)	
Shares used to compute basic and diluted net loss per share	14,813,156	12,410,576	12,105,835	12,072,027	11,752,139	





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	As of December 31,				
	2011	2010	2009	2008	2007
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and current investment securities	\$ 15,093	\$ 28,252	\$ 43,497	\$ 19,297	\$ 70,635
ARS put current			2,557		
Restricted cash, investment and letter of credit- current		29,313			
Working capital	12,010	21,554	24,500	17,836	65,938
Restricted cash, investment and letter of credit- long-term			31,223		
Investment-long-term			2,085	24,047	
ARS put long-term				5,793	
Total assets	30,787	72,934	94,327	50,224	73,752
Current portion of long-term debt		4,952			
Long-term debt, less current portion		9,484			
ARS loan payable			17,605		
Convertible notes		28,626	29,258		
Deficit accumulated during the development stage	(285,272)	(267,538)	(247,351)	(226,982)	(205,057)
Total stockholders equity	23,498	24,704	40,013	48,045	66,608

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### **Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.**

*You should read the following discussion and analysis together with Item 6. Selected Financial Data and the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth under the caption Item 1A. Risk Factors.*

#### **Overview**

#### **Background**

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. We were incorporated in Delaware in September 2000.

We have incurred significant net losses since our inception. At December 31, 2011, from inception, our accumulated deficit was approximately \$285.3 million, including approximately \$49.7 million of non-cash stock-based compensation charges related to employee stock-based compensation and founders' warrants. We expect to incur substantial net losses for the next several years as we continue to develop certain of our existing product development programs, primarily MN-221 for the treatment of acute exacerbations of asthma and COPD exacerbations, and over the long-term if we are successful in expanding our research and development programs and acquiring or in-licensing products, technologies or businesses that are complementary to our own. While there can be no assurances, we believe our working capital at December 31, 2011 to be sufficient to fund our operating requirements for at least through December 31, 2012.

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, bronchial asthma, 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 COPD exacerbations.

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. In accordance with the joint venture agreement, on March 16, 2012, we paid \$650,000 for our 30% interest in the joint venture company. The other parties to the joint venture agreement are responsible for providing their initial funding in the joint venture company for their combined 70% interest, and for future funding for the joint venture company's activities which will include managing and operating a facility to manufacture drug candidates for the Chinese market, promoting, distributing and selling drug candidates in the Chinese market and conducting clinical trials necessary to gain regulatory approval in China. The joint venture company will initially conduct these activities with respect to MN-221, however other drug candidates may be brought within the scope of the joint venture company if the parties to the agreement unanimously agree. 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. At December 31, 2011, we reflect a long-term asset on our consolidated balance sheet which represents our investment and a corresponding current liability which represents our required capital contribution payable to the joint

venture company. We evaluated the joint

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venture company under the authoritative guidance and concluded that it is a variable interest entity for which we are not the primary beneficiary as we will not have a majority of the board seats and we will not have any power to direct or significantly influence the actions of the entity. We will therefore not consolidate the joint venture company into our financial results but will account for the activities of the joint venture company under the equity method whereby we will absorb any loss or income generated by the entity according to our percentage ownership.

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

MN-221 for the treatment of acute exacerbations of asthma and COPD exacerbations, for which we initiated a Phase 2 clinical trial (MN-221-CL-007) in the first quarter of 2009 to evaluate the safety and efficacy of MN-221 in patients with acute exacerbations of asthma treated in the emergency room. This trial completed enrollment in March 2012. Depending on the results of our Phase 2 clinical trial (MN-221-CL-007) 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. COPD development, which included a Phase 1b clinical trial in patients with stable, moderate to severe COPD, was completed in 2010. In the first quarter of 2012 we initiated an additional Phase 1b/2a COPD clinical trial that has commenced enrollment and has an anticipated trial completion around the end of the second quarter of 2012.

MN-166, an ibudilast-based product development, for which we continue to pursue discussions with potential partners or other strategic collaboration(s). MN-166 has completed a Phase 2 clinical trial in MS in Eastern Europe in 2008 wherein positive safety and neuroprotective efficacy indicators were obtained, thus, directing next stage development towards a Phase 2b progressive MS indication. Limited animal safety and product manufacturing and stability work has been completed or is ongoing. In the drug addiction area, a Phase 1b/2a opioid withdrawal clinical trial funded by the National Institute on Drug Abuse, or NIDA, was completed at the end of 2010. A Phase 1b NIDA-funded clinical trial in methamphetamine-dependent volunteers with expert investigators at UCLA initiated in the fourth quarter of 2010 and is currently enrolling patients. In addition, a headache and pain specialist in Australia initiated an investigator sponsored Phase 2 clinical trial of ibudilast as a potential new pharmacotherapy for medication overuse headache that is expected to complete enrollment at the end of 2012. We intend to enter into additional strategic alliances with leading pharmaceutical or biotech companies to support further clinical development of MN-166.

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, and to keep certain commercialization rights in select markets. Depending on the outcome of the Phase 2 trial of MN-221 for the treatment of acute exacerbations of asthma, we may seek to raise additional capital and/or enter into a collaboration and conduct a Phase 3 development program. 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 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 development programs, we plan to conduct development activities only to the extent deemed necessary to maintain our license rights or maximize its value while pursuing a variety of initiatives to monetize such programs.

Our eight non-prioritized 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;

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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 the treatment of generalized anxiety disorder/insomnia, 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.

***Avigen Transaction***

On December 18, 2009, we acquired Avigen a biopharmaceutical company that focused on identifying and developing differentiated products to treat patients with serious disorders, whose potential product candidate is a microphage migration inhibitor and a glial attenuator for central nervous system, or CNS, disorders such as neuropathic pain, and opioid addiction and withdrawal and methamphetamine addiction. We continue to pursue discussions with potential partners to secure a strategic collaboration to advance clinical development of the combined development programs.

Absolute Merger, Inc., a wholly-owned subsidiary of ours, merged with and into Avigen. Under the terms of the merger, we issued approximately \$29.4 million in secured convertible notes that matured on June 18, 2011, the 18-month anniversary of the closing of the merger. Holders of these convertible notes could convert their notes into our common stock at an initial conversion price of \$6.80 per share through May 31, 2011. At the maturity of the convertible notes, the remaining holders would be paid the same per share amount as the Avigen shareholders that elected to receive cash at the merger closing plus accrued interest, approximately \$1.19 per share. As part of the merger consideration, the former Avigen shareholders were also entitled to receive approximately \$0.04 per share, which was paid in two increments in 2010, and rights under contingent payment rights, or CPR, issued as part of the merger consideration. In March 2011 we paid \$0.02 per share to former Avigen shareholders related to the management transition plan CPR. All additional CPR expired on August 18, 2011 and no payments were made related to these CPR.

Our consolidated financial statements include Avigen's operations following the completion of the Avigen merger. We accounted for the Avigen merger using the acquisition method of accounting. As a result, we recorded \$4.8 million of IPR&D related to Avigen's product candidate asset and \$9.6 million of goodwill related to the excess purchase price over the assigned values of the net assets acquired. The goodwill was primarily a result of the conversion feature related to the convertible notes issued pursuant to the merger agreement. Our annual test date for IPR&D and goodwill impairment is December 31. During the year ended December 31, 2011 and through the date of this report, there were no triggering events, market conditions or other factors (such as adverse clinical trial results) that would indicate possible or actual impairment of IPR&D or

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goodwill. Since we operate under one reporting segment, goodwill impairment is assessed on our overall market capitalization. We did not record goodwill impairment during the year ended December 31, 2011 since at year-end the Company's total market capitalization was in excess of the carrying value of its net assets. Based on our assessment of IPR&D using an income approach, we also did not record impairment of IPR&D during the year ended December 31, 2011.

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### ***Convertible Notes***

At the closing of the Avigen merger, we and American Stock Transfer & Trust Company, LLC, as trustee, entered into an indenture. Under the terms of a separate trust agreement, or Trust Agreement, approximately \$29.4 million, which represented the First Payment Consideration less approximately \$6.0 million paid out to Avigen shareholders who elected cash payment and the initial principal amount of the convertible notes, or Convertible Notes, was deposited with a trust agent for the benefit of the holders and us.

Prior to the maturity of the convertible notes on June 18, 2011, holders of the Convertible Notes could submit irrevocable conversion notices instructing the trustee to convert such Convertible Notes into shares of our common stock at an initial conversion price of \$6.80 per share. Following each conversion date we would issue the number of whole shares of common stock issuable upon conversion and the trustee would in turn release to us the respective amount of restricted cash to cover the stock issuance. For the year ended December 31, 2011, approximately \$76,000, of Convertible Notes were converted into 11,246 shares of our common stock. All remaining Convertible Notes matured on June 18, 2011 and the principal was repaid in full.

### ***Debt***

On May 10, 2010, we entered into a loan and security agreement, or the Loan Agreement, with Oxford Finance Corporation, or Oxford, under which we borrowed \$15.0 million at a stated annual interest rate of 12.87%. The financing was used to satisfy working capital needs, including the continued clinical development of MN-221. Pursuant to the Loan Agreement, we issued to Oxford a warrant to purchase up to 198,020 shares of our common stock, par value \$0.001 per share, at an exercise price of \$6.06 per share. Based on a Black-Scholes valuation model, the relative fair value of the warrant was approximately \$859,000. We accounted for the warrant as a component of stockholders' equity as the agreement required settlement in shares and under no provision of the agreement were we required to settle the warrant in cash.

We accounted for the interest on the debt under the effective interest method wherein we treated the debt issuance costs paid directly to the lender and the relative fair value of the warrants issued to the lender as a discount on the debt (or a contra liability) and we treated the debt issuance costs paid to third parties as an asset. The amortization of the debt discount was recorded as interest expense and the amortization of the debt issuance costs paid to third parties was recorded as other expense in our consolidated statement of operations.

On April 1, 2011, we entered into an agreement with Oxford under which we made an early repayment of the loan in-full and wherein Oxford waived the prepayment penalty of approximately \$437,000.

### ***Reduction-in-Force***

In January 2011, we had a reduction-in-force, or RIF, to reduce costs. We believe that we remain adequately staffed given our research and development focus and utilization of external resources.

### ***Underwritten Firm Commitment Public Offering***

On March 23, 2011, we consummated a firm-commitment underwritten public offering of 2,750,000 units at a price to the public of \$3.00 per unit for gross proceeds of approximately \$8.25 million. Each unit consists of one share of common stock, and a warrant to purchase one share of common stock. The shares of common stock and warrants are immediately separable and were issued separately. On March 24, 2011, the underwriter exercised 50,666 units of its 412,500 unit over-allotment. The warrants are exercisable immediately upon issuance, have a five-year term and an exercise price of \$3.56 per share. The warrants are indexed to our stock and do not permit net-cash settlement. On March 29, 2011, we received net proceeds of approximately \$7.7 million, after underwriter discount and underwriter expenses and no warrants exercised. In accordance with the authoritative guidance, the warrants were classified as equity instruments as they contain no provision which may require cash settlement.



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### ***At-The-Market Issuance Sales Agreement***

On May 5, 2011, we entered into an at-the-market (or ATM) issuance sales agreement, or sales agreement, with McNicoll, Lewis & Vlak LLC, or MLV, pursuant to which we could issue and sell shares of our common stock having an aggregate offering price of up to \$15.0 million from time to time through MLV as our sales agent. The issuance and sale of these shares by us under the sales agreement, if any, would be subject to the effectiveness of our shelf registration statement on Form S-3 (File No. 333-163116), initially filed with the Securities and Exchange Commission on November 13, 2009.

Effective October 23, 2011, we terminated the ATM between us and MLV. No shares of common stock were issued under the ATM.

### ***Lease Amendments***

On July 6, 2011, we entered into a fifth amendment, or the Fifth Lease Amendment, of our lease agreement with 4350 La Jolla Village LLC, the Landlord. The Fifth Lease Amendment amends the Lease of our headquarters located at 4350 La Jolla Village Drive, Suite 950, San Diego, California, 92122, and extends the Lease term with respect to 5,089 square feet, from August 31, 2011 to May 31, 2012. The Fifth Lease Amendment provides that we will pay the Landlord a monthly base rent of \$12,468 for the premises during the nine-month extension period. On March 19, 2012, we entered into a sixth amendment, the Sixth Lease Amendment, of our lease agreement with 4350 the Landlord. The Sixth Lease Amendment extends the lease term through February 28, 2013 and provides that we will pay the Landlord a monthly base rent of \$12,672 for the premises during the final nine month period

### ***Kissei Stock Purchase***

On October 13, 2011, pursuant to a stock purchase agreement by and between us and Kissei Pharmaceutical Co., Ltd., or Kissei, Kissei purchased for \$7.5 million (i) an aggregate of 800,000 shares of our common stock, par value \$0.001 per share at a price of \$2.50 per share, which approximated the fair value of our common stock at the time of the transaction, and (ii) 220,000 shares of our Series B Convertible Preferred Stock, par value \$0.01 per share, at a price of \$25.00 per share, which approximated the fair value of our preferred stock on an as converted basis at the time of the transaction. Each share of the Series B Preferred Stock is convertible into 10 shares of Common Stock. The Purchase Agreement contained customary representations, warranties and covenants and a standstill agreement from Kissei that terminates if Kissei beneficially owned less than three percent of our outstanding voting stock.

### ***Kissei Services Agreement***

On October 13, 2011, we entered into an agreement with Kissei to perform research and development services relating to MN-221 in exchange for a non-refundable upfront payment of \$2.5 million. Under the terms of the agreement, we will be responsible for all costs to be incurred in the performance of these services which are expected to be completed in 2012 and 2013. We assessed the deliverables in accordance with the authoritative guidance and concluded the existence of one deliverable, research and development services. As such, we will recognize as revenue the \$2.5 million payment as the research and development services are performed. The amount received from Kissei is recorded on the balance sheet at December 31, 2011 as deferred revenue. As of December 31, 2011, we have not recorded any revenue in 2011 relating to this agreement.

*Revenues and Cost of Revenues*

We recognized no revenues for each of the years in the three-year period ended December 31, 2011. We have not generated any revenues from licensing, milestones or product sales to date. Our revenues to date have been generated from providing development management services under master service agreements with Asahi

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Kasei Pharma Corporation and Argenes, Inc., pursuant to which we billed consulting fees and our pass-through clinical contract costs. The primary costs associated with our revenue were the clinical contract costs we incurred and passed-through to our customers. Our agreement with Asahi Kasei Pharma Corporation has been completed, and we terminated our agreement with Argenes, Inc., and we will not generate any further revenue from these agreements.

**Research and Development**

Our research and development expenses consist primarily of the license fees related to our product candidates, salaries and related employee benefits, costs associated with the preclinical and clinical development of our product development programs, costs associated with non-clinical activities, such as regulatory expenses, and pre-commercialization manufacturing development activities. We use external service providers to manufacture our compounds to be used in clinical trials and for the majority of the services performed in connection with the preclinical and clinical development of our product candidates; therefore, these research and development expenses consist substantially of external costs, such as fees paid to consultants, contract research organizations, contract manufacturers and other external service providers, including professional fees and costs associated with legal services, patents and patent applications for our intellectual property. Internal research and development expenses consist of costs of compensation and other expenses for research and development personnel, supplies, materials, facility costs and depreciation. Research and development costs are expensed as incurred or accrued based on certain contractual factors such as for estimates of work performed, milestones achieved, patient enrollment and experience with similar contracts. As actual costs become known, accruals are adjusted. To date, our estimates have not differed significantly from the actual costs incurred.

The following table summarizes our research and development expenses for the periods indicated for each of our product development programs. To the extent that costs, including personnel costs, are not tracked to a specific product development program, such costs are included in the Unallocated category (in thousands):

<b>Product</b>		<b>Year ended December 31,</b>		
		<b>2011</b>	<b>2010</b>	<b>2009</b>
<b>Candidate</b>	<b>Disease/Indication</b>			
MN-221	Acute exacerbations of asthma and COPD	\$ 5,677	\$ 7,304	\$ 8,419
MN-166	Multiple sclerosis/other CNS disorders	804	885	635
MN-001	Bronchial asthma and Interstitial cystitis	93	49	64
MN-001	Interstitial cystitis	33	49	27
MN-029	Solid tumors	97	106	86
MN-305	Generalized anxiety disorder/Insomnia	1	9	(1)
MN-221	Preterm labor	5	7	