IDERA PHARMACEUTICALS, INC.
Form 10-K
March 10, 2010

Table of Contents

**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**

# FORM 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
**For the Fiscal Year Ended December 31, 2009**

**OR**

o **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: 001-31918**

**IDERA PHARMACEUTICALS, INC.**
**(Exact name of Registrant as specified in its charter)**

| **Delaware** | **04-3072298** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |
| **167 Sidney Street**<br>**Cambridge, Massachusetts**<br>**(Address of principal executive offices)** | **02139**<br>**(Zip Code)** |

**(617) 679-5500**
**(Registrant s telephone number, including area code)**

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

| **Title of Class:** | **Name of Each Exchange on Which Registered** |
|---|---|
| **Common Stock, $.001 par value**<br>**(Including Associated Preferred Stock Purchase Rights)** | **NASDAQ Global Market** |

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

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

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

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 the filing requirements for the past 90 days. Yes þ No o

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 o No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) 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. þ

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 the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

| Large accelerated filer o | Accelerated filer þ | Non-accelerated filer o | Smaller reporting company o |
|---|---|---|---|
| | | (Do not check if a smaller reporting company) | |

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

The approximate aggregate market value of the voting stock held by non-affiliates of the registrant was $133,031,000 based on the last sale price of the registrant s common stock as reported on the NASDAQ Global Market on June 30, 2009. As of February 26, 2010, the registrant had 23,488,925 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the Registrant s Proxy Statement with respect to the Annual Meeting of Stockholders to be held in June 2010 are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Form 10-K.

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**IDERA PHARMACEUTICALS, INC.**

**FORM 10-K**

**INDEX**



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Table of Contents

## FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, included or incorporated in this report regarding our strategy, future operations, collaborations, intellectual property, financial position, future revenues, projected costs, prospects, plans, and objectives of management are forward-looking statements. The words believes, anticipates, estimates, plans, expects, intends, may, could, should, potential, likely, projects, continue, will, and wo expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those set forth below under Part I, Item 1A Risk Factors. These factors and the other cautionary statements made in this Annual Report on Form 10-K should be read as being applicable to all related forward-looking statements whenever they appear in this Annual Report on Form 10-K. In addition, any forward-looking statements represent our estimates only as of the date that this Annual Report on Form 10-K is filed with the SEC and should not be relied upon as representing our estimates as of any subsequent date. We do not assume any obligation to update any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

Table of Contents

## PART I.

### Item 1. *Business*

### Overview

We are engaged in the discovery and development of DNA- and RNA-based drug candidates targeted to Toll-Like Receptors, or TLRs, to treat infectious diseases, autoimmune and inflammatory diseases, cancer, and asthma and allergies, and for use as vaccine adjuvants. Drug candidates are compounds that we are developing and that have not been approved for any commercial use. TLRs are specific receptors present in immune system cells that recognize the DNA or RNA of bacteria or viruses and initiate an immune response. Relying on our expertise in DNA and RNA chemistry, we have designed and created proprietary TLR agonists and antagonists to modulate immune responses. A TLR agonist is a compound that stimulates an immune response through the targeted TLR. A TLR antagonist is a compound that blocks activation of an immune response through the targeted TLR.

Our business strategy is to advance applications of our TLR-targeted drug candidates in multiple disease areas simultaneously. We are advancing some of these applications through internal programs, and we seek to advance other applications through collaborative alliances with pharmaceutical companies. Collaborators provide the necessary resources and drug development experience to advance our compounds in their programs. Upfront payments and milestone payments received from collaborations help to provide us with the financial resources for our internal research and development programs.

Our internal programs are focused on developing TLR-targeted drug candidates for the potential treatment of infectious diseases, autoimmune and inflammatory diseases, cancer, and asthma and allergies.

*Infectious disease program.* We are conducting two Phase 1 clinical trials of IMO-2125, a TLR9 agonist, in patients with chronic hepatitis C virus, or HCV, infection. In our first Phase 1 trial, we are evaluating IMO-2125 in patients with chronic HCV infection who had no response to a prior regimen of the current standard of care therapy. We refer to these patients as null responder HCV patients. We are conducting our second Phase 1 clinical trial of IMO-2125 in combination with ribavirin in patients with chronic HCV infection who have not received prior treatment for their HCV infection. We refer to these patients as treatment-naïve HCV patients.

*Autoimmune and inflammatory disease program.* We are conducting a Phase 1 clinical trial of IMO-3100, an antagonist of TLR7 and TLR9, in healthy subjects. We are also evaluating IMO-3100 and other antagonists of TLR7 and TLR9 in mouse models of lupus, rheumatoid arthritis, multiple sclerosis, psoriasis, colitis, pulmonary inflammation, and hyperlipidemia.

*Cancer program.* We are studying RNA-based compounds that act as agonists of TLR7 and/or TLR8, which we refer to as **s**tabilized **i**mmune **m**odulatory **RNA**, or SIMRA, compounds, in preclinical models of hematological cancers. In preclinical models, we have observed antitumor activity of a dual agonist of TLR7 and TLR8 as monotherapy and in combination with selected targeted drugs currently approved for cancer treatment.

*Respiratory disease program.* We currently are evaluating the next steps in developing IMO-2134, a TLR9 agonist, for respiratory diseases. IMO-2134 was created by us and selected by Novartis International Pharmaceutical, Ltd., or Novartis, as a lead drug candidate for asthma and allergies under our research collaboration with Novartis that was terminated by Novartis in February 2010. During the term of the research collaboration, Novartis initiated a Phase 1 clinical trial of IMO-2134.

In addition to our internal programs, we currently are collaborating with two pharmaceutical companies to advance other applications of our TLR-targeted compounds. We are collaborating with Merck KGaA for cancer treatment, excluding cancer vaccines, and with Merck & Co., Inc., or Merck & Co., for vaccine adjuvants in the fields of cancer, infectious diseases, and Alzheimer s disease. Merck KGaA is conducting clinical trials of IMO-2055, a TLR9 agonist, in head and neck cancer, colorectal cancer and non-small cell lung cancer. Merck KGaA and Merck & Co. are not related.

Table of Contents

**Our Business Strategy**

We believe that our drug candidates targeted to TLRs have broad potential applications in the treatment of infectious diseases, autoimmune and inflammatory diseases, cancer, and asthma and allergies, and as vaccine adjuvants. To develop the potential of our discoveries in multiple areas simultaneously, we are advancing some of these applications through internal programs and seeking to advance other applications through collaborations with pharmaceutical companies.

We have entered into collaborative alliances for application of our technology in multiple therapeutic areas. We believe that Merck KGaA and Merck & Co. provide the necessary resources and expertise to advance our programs with them. In addition, we have received upfront payments and milestone payments from Merck KGaA and Merck & Co. that have helped to finance our internal research and development programs. We may also receive additional payments if agreed upon milestones are achieved and royalties if any commercial products result from our collaborations. Our prior collaboration with Novartis provided the resources that led to the identification of a lead compound and initiation of a Phase 1 clinical trial.

As we continue to advance our clinical evaluation of IMO-2125 in chronic HCV infection, our clinical evaluation of IMO-3100 in autoimmune and inflammatory diseases, and our preclinical programs, we may enter into additional collaborations for one or more of these programs. In considering any future collaborations, we will assess the resources and expertise a potential collaborator may bring to the development and commercialization of our drug candidates.

We intend to stay at the forefront of TLR-based research and discovery by applying our chemistry-based approach to design and create novel and proprietary DNA- and RNA-based compounds targeted to TLRs. We use these compounds, which are synthetic chemical compounds, to populate our expanding research and development programs and to support our collaborations.

**Overview of the Human Immune System**

The immune system protects the body by working through various mechanisms to recognize and eliminate bacteria, viruses and other infectious agents, referred to as pathogens, and abnormal cells such as cancer cells. These mechanisms initiate a series of signals resulting in stimulation of the immune system in response to the pathogens or abnormal cells. The activities of the immune system are undertaken by its two components: the innate immune system and the adaptive immune system.

The role of the innate immune system is to provide a rapid, non-specific response to a pathogen or to abnormal cells in the body and to activate the adaptive immune system. The innate immune system consists of specialized cells such as macrophages, dendritic cells and monocytes. When the body recognizes a pathogen, it activates cells of the innate immune system, resulting in a cascade of signaling events that cause the production of proteins such as cytokines to fight the infection caused by the pathogen. Unlike the antibodies and cellular responses produced by the adaptive immune system as described below, the proteins produced by the innate immune system are not pathogen-specific. Moreover, once the pathogen is eliminated and the infection is resolved, the innate immune system will not remember the pathogen.

In contrast to the innate immune system, the adaptive immune system provides a pathogen-specific response to an infection. The adaptive immune system does this through the recognition by certain immune cells of specific proteins, called antigens, which are part of the pathogen or abnormal cell. Signals produced by the innate immune system initiate this process. Upon recognition of an antigen, which could come from pathogens or from cancer cells, the adaptive immune system produces antibodies and antigen-specific immune cells that specifically detect and destroy

cells that contain the antigen. This response is referred to as an antigen-specific immune response. An antigen-specific immune response normally takes several weeks to develop the first time. However, once developed, the adaptive immune system remembers the antigen. In this manner, if the pathogen again infects the body, the presence of the memory immunity will allow the adaptive immune system to respond again, this time in a matter of days.

Table of Contents

**TLR-based Drug Discovery Technology**

The human immune system is activated by recognizing pathogen-associated molecular patterns, or PAMPs. TLRs comprise a family of receptors that are known to recognize PAMPs. The different TLRs are expressed in various immune system cells and recognize different PAMPs. TLR9 is a receptor that specifically recognizes a PAMP that occurs in the DNA of bacteria and other pathogens, and compounds that mimic bacterial DNA. TLR7 and TLR8 are receptors that recognize viral RNA and compounds that mimic viral RNA.

Based on our extensive experience in DNA and RNA chemistry, we are designing and creating novel synthetic DNA- and RNA-based compounds, which as a chemical class are called oligonucleotides. Our compounds are designed to mimic the bacterial DNA and viral RNA that are recognized by TLR7, 8 or 9, with some of our compounds acting as agonists and others acting as antagonists.

*TLR9 Agonists*

Drug candidates that are agonists of TLR9 mimic bacterial DNA and induce immune responses through TLR9 that may be applicable to the treatment or prevention of infectious diseases, cancer, and asthma and allergies, and may be used as vaccine adjuvants. We have created our TLR9 agonist candidates to activate specific cells of the immune system and produce cytokines and other proteins. These activated cells and the cytokines and other proteins they produce lead to stimulation of both the innate and the adaptive components of the immune system. Furthermore, in preclinical cell culture and animal model studies, we have shown that we can change the immunological activity of our TLR9 agonists by modifying the chemical structure of the molecule. We are using our ability to change immunological activity of our TLR9 agonists to create a growing portfolio of drug candidates that are potentially useful for treating or preventing different diseases.

*TLR7 and TLR8 Agonists*

We are designing and creating novel synthetic RNA-based compounds that are agonists of TLR7 and/or TLR8, which we refer to as our SIMRA compounds. Our SIMRA compounds are designed to mimic viral RNA. In preclinical studies in cell culture and animal models, these TLR7 and/or TLR8 agonists induced immune responses that we believe may be applicable to the treatment of cancer and infectious diseases and as vaccine adjuvants. We are studying our TLR7 and TLR8 agonists in preclinical models of hematological cancers. In preclinical models, we have observed antitumor activity of these compounds as a monotherapy and in combination with selected targeted drugs currently approved for cancer treatment.

*TLR7 and TLR9 Antagonists*

We are creating novel classes of drug candidates that are designed to be antagonists of TLR7 and TLR9. Preclinical studies from independent researchers have suggested TLR7 and TLR9 may play a role in some autoimmune and inflammatory diseases. In cell-based experiments and animal models, our antagonists have blocked immune stimulation in the presence of specific agonists of TLR7 and specific agonists of TLR9. We have evaluated some of our antagonist drug candidates in preclinical mouse models of human autoimmune and inflammatory diseases including lupus, rheumatoid arthritis, multiple sclerosis, psoriasis, colitis, pulmonary inflammation, and hyperlipidemia. In these models, treatment with our antagonist drug candidates was associated with improvement in a number of disease parameters.

Table of Contents

**Research and Development Programs**

We and our collaborators are engaged in the evaluation of TLR-targeted drug candidates in multiple therapeutic areas. The following table summarizes the disease areas and the development status of our programs.

***INTERNAL RESEARCH AND DEVELOPMENT PROGRAMS***

| Drug candidate(s) | Disease Area | Development Status |
|---|---|---|
| *Infectious Diseases* | | |
| IMO-2125 (TLR9 agonist) | Chronic Hepatitis C Virus Infection | |
| | Null responder patients Treatment naïve patients | Phase 1 Clinical Trial Ongoing<br>Phase 1 Clinical Trial Ongoing |
| TLR7, 8, and 9 agonists | Viral Infectious Diseases | Research |
| *Autoimmune and Inflammatory Diseases* | | |
| IMO-3100 (dual TLR7/TLR9 antagonist) | Healthy Subjects | Phase 1 Clinical Trial Ongoing |
| | Lupus, Rheumatoid Arthritis, Multiple Sclerosis, Psoriasis, Colitis, Hyperlipidemia | Research |
| *Cancer* | | |
| TLR7, TLR8 agonists | Hematological Cancers | Research |
| *Respiratory Diseases* | | |
| IMO-2134 (TLR9 agonist) | Asthma, Allergies | Phase 1 Clinical Trial Initiated by Novartis during the Collaboration Period |

***COLLABORATIVE ALLIANCES***

| Drug candidate(s) | Disease Area | Development Status |
|---|---|---|
| *Merck KGaA Cancer* | | |
| IMO-2055 (EMD 1201081) (TLR9 Agonist) | | |
| IMO-2055 | Squamous Cell Cancer of Head and Neck | Phase 2 Clinical Trial Ongoing |
| IMO-2055 in combination with Tarceva® and Avastin® | Non-small Cell Lung Cancer | Phase 1b Clinical Trial Ongoing |
| IMO-2055 in combination with Erbitux® and chemotherapy | Colorectal Cancer | Phase 1b Clinical Trial Ongoing |
| *Merck & Co. Vaccine Adjuvants* | | |
| TLR7, 8, and 9 agonists | Cancer, Infectious Diseases, Alzheimer s Disease | Research |

*Infectious Diseases*

We and others have conducted preclinical studies in human cell-based assays in which TLR agonists have activated cells of the immune system and induced these cells to secrete cytokines and other proteins that lead to further immune responses. We believe that certain agonists of TLRs 7, 8, and 9 can induce immune system responses, which may have potential therapeutic applicability in infectious diseases, including those caused by viruses.

Our most advanced TLR-targeted drug candidates in infectious diseases are our DNA-based TLR9 agonists, which have been shown to induce high levels of interferon-alpha in preclinical models. Interferon-alpha is a protein

Table of Contents

that has been recognized to stimulate the immune system and is a component of the current standard of care for chronic HCV infection.

*Hepatitis C IMO-2125.* Chronic HCV infection causes inflammation of the liver, which significantly increases the risk that a patient will develop liver failure or liver cancer. The World Health Organization has reported that HCV is responsible for more than 50% of all liver cancer cases and two-thirds of all liver transplants in the developed world. The World Health Organization has estimated that about 200 million people are chronically infected with HCV worldwide and that an additional 3 million to 4 million people are infected each year. The Centers for Disease Control and Prevention have estimated that approximately 3 million people in the United States are chronically infected with HCV. Genotype 1 HCV, which is the type of HCV most resistant to current standard of care therapy, is the most prevalent form of HCV in the United States, Europe, and Japan. Currently, the standard of care treatment for chronic HCV infection is based on combination therapies that include a single recombinant interferon-alpha protein plus ribavirin, an antiviral medication.

We and other independent researchers have shown in preclinical studies that TLR9 agonists induce many proteins, including natural interferon-alpha proteins and other proteins with antiviral activity. We believe that the combined effect of these natural interferon-alpha proteins and other antiviral proteins may produce a broader or stronger antiviral effect than is obtained with a single recombinant interferon-alpha protein.

We have selected IMO-2125, a synthetic DNA-based TLR9 agonist, as our lead candidate for the treatment of chronic HCV infection. In preclinical models, including cultures of human immune cells and in nonhuman primates, IMO-2125 induced high levels of natural interferon and other antiviral proteins. The proteins induced by IMO-2125 in human immune cell cultures and in plasma from non-human primates dosed with IMO-2125 showed potent activity for inhibiting HCV RNA production in cell-based assays.

In May 2007, we submitted an Investigational New Drug, or IND, application for IMO-2125 to the United States Food and Drug Administration, or FDA. In September 2007, we initiated a Phase 1 clinical trial of IMO-2125 in patients with genotype 1 chronic HCV infection who had no response to a prior regimen of the current standard of care therapy. We refer to these patients as null responder HCV patients. The clinical trial is currently being conducted at six sites in the United States. In the trial, we are enrolling cohorts of ten patients at escalating IMO-2125 dose levels. To date, we have enrolled patients in four cohorts, evaluating IMO-2125 at 0.04 mg/kg/week, 0.08 mg/kg/week, 0.16 mg/kg/week and 0.32 mg/kg/week. Based on interim results from these cohorts, we extended the trial to a fifth dose level and are currently enrolling patients in a fifth cohort at 0.48 mg/kg/week. Of the ten patients in a cohort, eight are randomized to receive IMO-2125 treatment and two are randomized to receive placebo treatment. Patients receive a single dose of IMO-2125 or placebo once per week by subcutaneous injection for four weeks. The primary objective of the trial is to assess the safety of IMO-2125 at each dose level. We are also evaluating the effects of IMO-2125 on HCV RNA levels and on immune system activation in this trial.

In December 2009, we announced interim results from null responder HCV patients treated through the originally planned four cohorts of this trial. IMO-2125 was well tolerated by all patients in the four cohorts. IMO-2125-treated patients showed dose-dependent increases in natural interferon-alpha and other antiviral proteins including interferon-inducible protein 10 and 2 ,5 -oligoadenylate synthetase. In addition, an increasing percentage of patients, ranging from 40% at the 0.08 mg/kg/week dose level to 75% at the 0.32 mg/kg/week dose level, achieved a maximum reduction in viral load of 1 log10 or more at least once during the four-week treatment period. In contrast, none of the patients who received placebo treatment or IMO-2125 at the 0.04-mg/kg/week dose level achieved a maximum reduction in viral load of 1 log10 or greater at any time during the four-week treatment period. We plan to present detailed interim results of the trial at a scientific meeting in the second quarter of 2010.

In addition to the on-going Phase 1 clinical trial of IMO-2125 in null responder HCV patients, we are conducting a Phase 1 clinical trial of IMO-2125 in combination with ribavirin, an antiviral medication approved for use in combination with interferon-alpha in the treatment of HCV infection, in treatment-naïve patients with genotype 1 chronic HCV infection. We initiated the trial in October 2009. In this clinical trial, patients will receive IMO-2125 or a control article by subcutaneous injection once per week for four weeks at escalating dose levels in combination with daily oral administration of standard doses of ribavirin. A total of 15 patients are planned for the first cohort, with 12 randomized to receive IMO-2125 and ribavirin and three randomized to receive placebo and ribavirin as the control. Starting with the second cohort, 12 patients will be randomized to receive IMO-2125 and

Table of Contents

ribavirin and six patients will be randomized to receive pegylated recombinant alfa-2a interferon and ribavirin as the control. The primary objective of the trial is to assess the safety and tolerability of IMO-2125 in combination with ribavirin. In addition, we plan to monitor the effect of treatment on HCV RNA levels. The clinical trial is currently being conducted at sites in France and Russia.

We have formed a Hepatitis C Clinical Advisory Board to advise us on the clinical development of IMO-2125 for the treatment of chronic HCV infection. Members of our Hepatitis C Clinical Advisory Board include leading hepatologists from Europe and the United States.

Following the completion of our Phase 1 study in null responder HCV patients, we plan to initiate in the second half of 2010 a clinical trial in which null responder HCV patients will receive IMO-2125 in combination with ribavirin for 12 weeks. With the data from this trial, together with the data from the two Phase 1 clinical trials, we plan to determine the next steps in the clinical development of IMO-2125 for HCV infection.

*Viral Diseases.* In addition to our TLR9 agonists such as IMO-2125, we have developed synthetic RNA-based compounds that mimic viral RNA and induce immune responses by functioning as agonists of TLR7 and/or TLR8. We are actively researching these compounds, and in human cell-based assays and *in vivo* in non-human primates, these compounds have induced immune responses that may be applicable to the treatment of viral infectious diseases.

*Autoimmune and Inflammatory Diseases*

In autoimmune diseases such as lupus, psoriasis, and rheumatoid arthritis, the immune system forms autoantibodies to a molecule that is a normal part of the body. The autoantibodies may bind RNA, DNA, or complexes that contain RNA or DNA. Independent researchers have reported that TLR7 and TLR9 may recognize autoantibody complexes that contain RNA or DNA and induce further immune responses that include cytokine production, inflammation, and tissue damage. Independent researchers have also reported that patients with autoimmune diseases such as lupus, psoriasis, and rheumatoid arthritis have increased incidence of hyperlipidemia and other cardiovascular risk factors.

We have identified DNA-based compounds that in preclinical studies have acted as antagonists of TLR7 and TLR9. We believe that these antagonists may have application in the treatment of autoimmune diseases by inhibiting TLR7- or TLR9-mediated responses to the immune complex and thereby interfering with the inflammatory disease progression caused by activation of the immune system. Additionally, we believe that TLR antagonists may have application in the treatment of hyperlipidemia and other cardiovascular risk factors associated with some autoimmune diseases.

We have conducted evaluations of these compounds in various preclinical studies, including in strains of mice that are genetically predisposed to develop autoimmune disease similar to the human autoimmune disease lupus, in a mouse model of rheumatoid arthritis, in a mouse model of multiple sclerosis, in mouse models of psoriasis, in a mouse model of colitis, and in a mouse model of pulmonary inflammation. Data from each of these evaluations showed improvement in a number of disease parameters.

In August 2008, we selected IMO-3100 as a lead antagonist drug candidate and initiated preclinical development studies.

In October 2009, at the Annual Scientific Meeting of the American College of Rheumatology and Association of Rheumatology Health Professionals, we presented preclinical data from studies of IMO-3100 in combination with Enbrel®, an inhibitor of tumor necrosis factor alpha currently used for the treatment of rheumatoid arthritis. In a mouse model of collagen-induced arthritis, mice treated with a combination of IMO-3100 and Enbrel had lower arthritic scores, less inflammation, and less abnormal bone pathology as compared to mice treated with either agent

alone. The data also showed that the activity of a low Enbrel dosage was markedly enhanced when combined with IMO-3100 in this mouse model.

In February 2010 we presented data from a preclinical study that evaluated the pharmacodynamic mechanism of action of IMO-3100 in non-human primates. In this study, we assessed the response of peripheral blood mononuclear cells, or PBMCs, to TLR7 and TLR9 agonists at various times after subcutaneous administration of

Table of Contents

IMO-3100 to non-human primates. Subcutaneous treatment with IMO-3100 was shown to inhibit induction of various cytokines and chemokines by TLR7 and TLR9 agonists in PBMC cultures, compared with PBMCs from blood samples taken prior to the dosing of IMO-3100. This inhibition was dependent on both the dosage of IMO-3100 administered and the time after administration of IMO-3100. IMO-3100 inhibition was specific to TLR7 and TLR9.

In November 2009, we submitted to the FDA an IND application for the clinical evaluation of IMO-3100 in autoimmune diseases. In January 2010, we initiated a Phase 1 clinical trial of IMO-3100 in healthy subjects. In this rising single-dose Phase 1 trial, IMO-3100 is being administered by subcutaneous injection. The primary objective is to evaluate safety and tolerability of IMO-3100. Secondary objectives are to characterize the pharmacokinetic profile of IMO-3100 and to assess the pharmacodynamic mechanism of action through measurement of the response of PBMCs to TLR7 and TLR9 agonists. The trial is being conducted at a single U.S. site.

We plan to use the results from this rising single-dose clinical trial to select dosages for an anticipated follow-up trial in healthy subjects. The purpose of the second Phase 1 trial would be to evaluate the safety, pharmacokinetics and pharmacodynamic mechanism of action of IMO-3100 with escalating doses in a study involving the subcutaneous administration of IMO-3100 once per week for four weeks. We intend to identify an initial autoimmune disease indication for further clinical development of IMO-3100 by the end of 2010.

We have formed an Autoimmune Disease Scientific Advisory Board with leading researchers in the field of autoimmune diseases to assist us with determining a clinical development strategy for our antagonist candidates.

*Cancer*

The immune system is capable of recognizing cancer cells as abnormal cells, leading to an immune response. However, the body s immune response to cancer cells may be weak or absent. We believe that agonists of TLR7, TLR8, and TLR9 can enhance the body s immune response to cancer cells because TLRs are involved in stimulation of both innate and adaptive immunity.

We have licensed our rights to the use of TLR9 agonists for the treatment of cancer under our collaboration with Merck KGaA, and are exploring on our own the use of TLR7 and TLR8 agonists for the treatment of cancer. We have created synthetic SIMRA compounds that mimic viral RNA and induce immune responses by functioning as agonists of TLR7 and TLR8. We are studying our SIMRA compounds in preclinical models of hematological cancers. In these preclinical models, we have observed antitumor activity of these compounds as a monotherapy and in combination with selected targeted drugs currently approved for cancer treatment.

*Respiratory Diseases*

Asthma and allergy conditions are characterized by an imbalance of the immune system. Currently approved agents for the treatment of asthma and allergy conditions, including steroids and antibodies, are generally designed to suppress symptoms of asthmatic or allergic response. Our TLR9 agonists, by comparison, are designed to induce immune responses that could be useful in restoring immune system balance. In preclinical studies conducted by us and our collaborators, our TLR9 agonists caused improvements in multiple indices of allergic conditions. For example, in mouse models of allergy, our TLR9 agonists restored the balance of immunological activity, produced a higher ratio of specific versus non-specific antibodies, reduced the number of pulmonary immune cells that produce allergic inflammation, and improved lung function.

In May 2005, we entered into a research collaboration and option agreement and a separate license, development, and commercialization agreement with Novartis to discover, optimize, develop and commercialize TLR9 agonists as treatments for asthma and allergies. In September 2008, Novartis initiated a Phase 1 clinical trial of QAX935, a novel

agonist of TLR9. Novartis terminated the research collaboration and option agreement, effective as of February 2010. This termination cancels Novartis option to implement the license, development and commercialization agreement. In connection with the termination, we regained all rights to QAX935, which we refer to as IMO-2134, without any financial obligations to Novartis, and are no longer subject to restrictions under the Novartis agreements on our right to develop TLR-targeted compounds, including TLR antagonist and TLR

antisense compounds, for respiratory diseases. Sponsorship of the trial initiated by Novartis has not been transferred to us. We are developing a strategy to advance the clinical development of IMO-2134 in asthma and allergy.

*Collaborative Alliances*

*Cancer Merck KGaA*

In December 2007, we entered into an exclusive, worldwide license agreement with Merck KGaA to research, develop, and commercialize products containing our TLR9 agonists, including IMO-2055, for the treatment of cancer, excluding cancer vaccines. Merck KGaA refers to IMO-2055 as EMD 1201081.

Prior to entering into our agreement with Merck KGaA, we had commenced clinical trials of IMO-2055, including a Phase 1b clinical trial of IMO-2055 in patients with non-small cell lung cancer. In January 2009, we initiated a Phase 1b clinical trial of IMO-2055 in patients with colorectal cancer. In April 2009, we initiated on behalf of Merck KGaA a Phase 1 clinical trial of IMO-2055 in healthy subjects. Merck KGaA agreed to reimburse us for costs associated with trials that we initiated and conducted, including costs associated with the Phase 1b clinical trials of IMO-2055 in patients with non-small cell lung cancer and in patients with colorectal cancer and the Phase 1 clinical trial of IMO-2055 in healthy subjects, that were incurred after February 4, 2008, which is the date our agreement with Merck KGaA became effective. In September 2009, Merck KGaA assumed sponsorship of our ongoing Phase 1b clinical trials of IMO-2055. Merck KGaA is now the sponsor of all clinical trials of IMO-2055 for the treatment of cancer and has assumed responsibility for all further clinical development of IMO-2055 in the treatment of cancer, excluding vaccines.

*Ongoing Clinical Trials of IMO-2055*

*Squamous Cell Carcinoma of the Head and Neck Phase 2 Clinical Trial.* In December 2009, Merck initiated a Phase 2 clinical trial of IMO-2055 in patients with recurrent or metastatic squamous cell carcinoma of the head and neck. Under the terms of our agreement with Merck KGaA, we received a milestone payment of 3.0 million (approximately $4.1 million) from Merck KGaA in the first quarter of 2010 related to the initiation of this Phase 2 clinical trial of IMO-2055.

*Non-small Cell Lung Cancer Avastin and Tarceva Combination Phase 1b Clinical Trial.* In December 2007, we initiated a Phase 1b clinical trial of IMO-2055 in combination with Avastin and Tarceva, agents approved for the treatment of specific cancers, in patients with non-small cell lung cancer whose cancer had progressed during a prior course of standard therapy. We designed the trial to assess the safety of IMO-2055 in combination with standard dosages and schedules of Tarceva and Avastin and to determine the recommended dosage of IMO-2055 for potential use in a subsequent Phase 2 trial. In the trial, IMO-2055 was administered at four escalating dose levels of 0.08, 0.16, 0.32, and 0.48 mg/kg/week with fixed standard dose regimens of Avastin and Tarceva. Patients received IMO-2055 subcutaneously once a week, with each patient continuing to receive therapy until disease progression as determined by Response Evaluation Criteria in Solid Tumors, or RECIST, or another protocol-specified stopping criterion was met. In September 2009, we reported preliminary data from the dose-escalation portion of the trial. The combination of IMO-2055 with Avastin and Tarceva was well tolerated at all dose levels, and eight of the 16 patients enrolled in the dose-escalation portion of the trial remained on treatment for at least 18 weeks. Of the 13 patients evaluable for tumor response in the dose-escalation portion of the trial, three had a partial response and eight experienced stable disease. Based on the dose escalation portion of the trial, Merck KGaA selected a dose level of IMO-2055 for expanded patient recruitment to evaluate further the safety and pharmacokinetics of the combination.

*Colorectal Cancer Erbitux and Chemotherapy Combination Phase 1b Clinical Trial.* In January 2009, we initiated a Phase 1b clinical trial of IMO-2055 in combination with Erbitux and chemotherapy in patients with colorectal cancer

whose cancer had progressed during a prior course of standard therapy. We designed the trial to assess the safety of the IMO-2055, Erbitux, and chemotherapy combination and to determine the recommended dosage of IMO-2055 for potential use in a subsequent Phase 2 clinical trial. This trial was designed with a target enrollment of up to 50 patients. Under the protocol for the trial, IMO-2055 is being administered at three escalating dose levels with fixed standard dose regimens of Erbitux and chemotherapy. Patients are receiving IMO-2055

Table of Contents

subcutaneously once a week, with each patient continuing to receive therapy until disease progression, as determined by RECIST, or another protocol-specified stopping criterion is met.

*Prior Clinical Trials of IMO-2055.*

In April 2009, we initiated on behalf of Merck KGaA a Phase 1 clinical trial of IMO-2055 monotherapy in healthy subjects. The Phase 1 healthy subjects trial was designed to characterize further the pharmacokinetic and pharmacodynamic profiles of IMO-2055 after single and multiple weekly subcutaneous and intravenous administrations. All scheduled patient visits were completed by June 2009.

Prior to entering our collaboration with Merck KGaA, we conducted three Phase 1 clinical trials and one Phase 2 clinical trial of IMO-2055. The Phase 1 clinical trials included a rising dose trial in healthy subjects, a rising dose trial in advanced cancer patients, and a combination trial of IMO-2055 with gemcitabine and carboplatin chemotherapy in advanced cancer patients. The Phase 2 clinical trial was a Phase 2 Stage A clinical trial of IMO-2055 monotherapy in patients with metastatic or recurrent clear cell renal cancer. The study contained four arms, comprised of a total of 89 treatment-naïve and second-line patients randomly assigned to receive IMO-2055 subcutaneously at either 0.16 mg/kg/week or 0.64 mg/kg/week. The primary objective of the study was tumor response based on RECIST. Secondary objectives included time to progression, survival and safety. Progression-free survival was also analyzed. The primary objective was not achieved in the study. However, the median progression-free survival was 4.5 months and 1.9 months for the 0.16- and 0.64-mg/kg/week treatment-naïve patients, and 3.4 months and 4.3 months for the 0.16- and 0.64-mg/kg/week second-line patients. The median overall survival was 23.5 months over all arms and 58% of patients had stable disease. Two patients (one second-line and one treatment-naïve, and each receiving 0.64 mg/kg/week) had confirmed partial responses, and seven patients received weekly IMO-2055 treatment for at least one year. IMO-2055 treatment was generally well-tolerated with good dose intensity in all arms of the study.

*Vaccine Adjuvants Merck & Co.*

Vaccines are composed of one or more antigens and one or more adjuvants in an appropriate formulation. The function of the adjuvants is to enhance immune recognition of the antigens and increase the ability of the immune system to make antigen-specific antibodies.

In preclinical animal models, our TLR agonists have shown adjuvant activity when combined with various types of antigens. Preclinical studies that we conducted with our TLR9 agonists and various antigens have shown improvements in several measures of antigen recognition, such as achievement of higher antibody levels, higher ratios of specific to nonspecific antibodies, and a reduction in the number of doses required to achieve effective antibody levels. As a result, we believe that TLR agonists have the potential to be used as adjuvants in vaccines.

In December 2006, we entered into a research collaboration with Merck & Co. and granted Merck & Co. an exclusive license to develop and commercialize our TLR7, 8, and 9 agonists by incorporating them in therapeutic and prophylactic vaccines being developed by Merck & Co. for cancer, infectious diseases, and Alzheimer s disease. The original term of the research collaboration was two years and Merck & Co. had the right to extend the research collaboration for two additional one-year periods. In November 2008, Merck & Co. extended the research collaboration for an additional year to December 2009, and in November 2009, Merck & Co. extended the research collaboration for the fourth and final year to December 2010. Merck & Co. is conducting preclinical studies to evaluate use of our TLR7, 8, and 9 agonists as vaccine adjuvants. In May 2008, we achieved a preclinical milestone under our collaboration with Merck & Co. involving one of our novel TLR9 agonists used as an adjuvant in cancer vaccines.

**Collaborative Alliances**

An important part of our business strategy is to enter into research and development collaborations, licensing agreements, and other strategic alliances with biotechnology and pharmaceutical corporations that bring expertise and resources to the potential development and commercialization of drugs based on our technology. We are currently a party to collaborations with Merck KGaA and Merck & Co.

Table of Contents

*Merck KGaA*

In December 2007, we entered into an exclusive, worldwide license agreement with Merck KGaA to research, develop and commercialize products containing our TLR9 agonists for the treatment of cancer, excluding cancer vaccines. Under the terms of the agreement, we granted Merck KGaA worldwide exclusive rights to our lead TLR9 agonists, IMO-2055 and IMO-2125, and to a specified number of novel follow-on TLR9 agonists to be identified by Merck KGaA and us under a research collaboration, for use in the treatment, cure and delay of the onset or progression of cancer in humans. Under the terms of the agreement:

- In February 2008, Merck KGaA paid us a $40.0 million upfront license fee in Euros of which we received $39.7 million due to foreign currency exchange rates;

- Merck KGaA agreed to reimburse future development costs for certain of our on-going IMO-2055 clinical trials, which we continued to conduct on behalf of Merck KGaA until September 2009;

- Merck KGaA agreed to pay us up to EUR 264 million in development, regulatory approval, and commercial success milestone payments if products containing our TLR9 agonist compounds are successfully developed and marketed for treatment, cure and/or delay of the onset or progression of cancer in humans; and

- Merck KGaA agreed to pay mid single-digit to low double-digit royalties on net sales of products containing our TLR9 agonists that are marketed.

We have agreed that neither we nor our affiliates will, either directly or through a third party:

- Develop or commercialize any TLR9 agonist for use in treating, curing, and delaying the onset or progression of cancer in humans; and

- Develop or commercialize IMO-2055 for use outside treating, curing, and delaying the onset or progression of cancer in humans, except as part of vaccine products in the fields of oncology, infectious diseases and Alzheimer s disease, which we are pursuing under our collaboration with Merck & Co.

These restrictions will not limit our ability to research, develop and commercialize vaccine products containing IMO-2055 in the fields of oncology, infectious diseases, and Alzheimer s disease, and to research, develop and commercialize IMO-2125 outside the licensed field as a combination therapy or as a vaccine product.

Under the agreement, Merck KGaA is obligated to pay us royalties, on a product-by-product and country-by-country basis, until the later of the expiration of the patent rights licensed to Merck KGaA and the 10th anniversary of the product s first commercial sale in such country. If the patent rights expire in a particular country before the 10th anniversary of the product s first commercial sale in such country, Merck KGaA s obligation to pay us royalties will continue at a reduced royalty rate until such anniversary. In addition, the applicable product royalties may be reduced if Merck KGaA is required to pay royalties to third parties for licenses to intellectual property rights. Merck KGaA s royalty and milestone obligations may also be reduced if Merck KGaA terminates the agreement based on specified uncured material breaches by us. The agreement may be terminated by either party based upon material uncured breaches by the other party or by Merck KGaA at any time after providing Idera with advance notice of termination.

In February 2009, we amended the license agreement with Merck KGaA so that we could initiate and conduct on behalf of Merck KGaA additional clinical trials of IMO-2055, until such time as Merck KGaA had filed an IND application with the FDA for IMO-2055 and assumed sponsorship of these trials. Under the amendment, Merck

KGaA agreed to reimburse us for costs associated with any additional trials that we initiated and conducted.

As of March 2010, Merck KGaA is now the sponsor of all clinical trials of IMO-2055 for the treatment of cancer and has assumed responsibility for all further clinical development of IMO-2055 in the treatment of cancer, excluding vaccines.

**Table of Contents**

*Merck & Co., Inc.*

In December 2006, we entered into an exclusive license and research collaboration agreement with Merck & Co. to research, develop and commercialize vaccine products containing our TLR7, 8,and 9 agonists in the fields of cancer, infectious diseases and Alzheimer s disease. Under the terms of the agreement, we granted Merck & Co. worldwide exclusive rights to a number of our TLR7, 8, and 9 agonists for use in combination with Merck & Co. s therapeutic and prophylactic vaccines under development in the fields of cancer, infectious diseases, and Alzheimer s disease. There is no limit to the number of vaccines to which Merck & Co. can apply our agonists within these fields. We also agreed with Merck & Co. to engage in a two-year research collaboration to generate novel agonists targeting TLR7 and TLR8 and incorporating both Merck & Co. and Idera chemistry for use in vaccines in the defined fields. Under the agreement, Merck & Co. had the right to extend the collaboration for two additional one-year periods. In November 2008, Merck & Co. extended the research collaboration for an additional year to December 2009, and in November 2009, Merck & Co. extended the research collaboration for the fourth and final year to December 2010.

Under the terms of the agreement:

- Merck & Co. paid us a $20.0 million upfront license fee;
- Merck & Co. purchased $10.0 million of our common stock at $5.50 per share;
- Merck & Co. agreed to fund the research and development collaboration;
- Merck & Co. agreed to pay us milestone payments as follows:
  - up to $165.0 million if vaccines containing our TLR9 agonist compounds are successfully developed and marketed in each of the oncology, infectious disease and Alzheimer s disease fields;
  - up to $260.0 million if vaccines containing our TLR9 agonist compounds are successfully developed and marketed for follow-on indications in the oncology field and if vaccines containing our TLR7 or TLR8 agonists are successfully developed and marketed in each of the oncology, infectious disease, and Alzheimer s disease fields; and
  - if Merck & Co. develops and commercializes additional vaccines using our agonists, we would be entitled to receive additional milestone payments; and
- Merck & Co. agreed to pay us mid to upper single-digit royalties on net product sales of vaccines using our TLR agonist technology that are developed and marketed, with the royalty rates being dependent on disease indication and the TLR agonist employed.

Under the agreement, Merck & Co. is obligated to pay us royalties, on a product-by-product and country-by-country basis, until the later of the expiration of the patent rights licensed to Merck & Co. and the expiration of regulatory-based exclusivity for the vaccine product. If the patent rights and regulatory-based exclusivity expire in a particular country before the 10th anniversary of the product s first commercial sale in such country, Merck & Co. s obligation to pay us royalties will continue at a reduced royalty rate until such anniversary, except that Merck & Co. s royalty obligation will terminate upon the achievement of a specified market share in such country by a competing vaccine containing an agonist targeting the same toll-like receptor as that targeted by the agonist in the Merck & Co. vaccine. In addition, the applicable royalties may be reduced if Merck & Co. is required to pay royalties to third parties for licenses to intellectual property rights, which royalties exceed a specified threshold. Merck & Co. s royalty and milestone obligations may also be reduced if Merck & Co. terminates the agreement based on specified uncured

material breaches by us.

Merck & Co. may terminate the collaborative alliance without cause upon 180 days written notice to us during the research term and upon 90 days written notice to us after the research term has ended. Either party may terminate the collaborative alliance upon the other party s filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or for a material breach if such breach is not cured within 60 days after delivery of written notice.

Table of Contents

Merck & Co. agreed, subject to certain exceptions, that for the duration of the research collaboration term, its ability to sell the shares of our common stock acquired by it under the agreement would be subject to specified volume limitations

**Antisense Technology**

We have been a pioneer in the development of antisense technology. We now are using our antisense expertise and technology to validate potential targets in the TLR signaling pathway, which may assist us in identifying drug candidates. We have identified antisense compounds targeted to human TLRs 2, 3, 4, 5, 6, 7, 8, and 9 and to the TLR-associated signaling protein MyD88. We are studying these compounds for potential applications in autoimmune and inflammatory diseases.

We also believe that our antisense technology may be useful to pharmaceutical and biotechnology companies that are seeking to develop drug candidates that down-regulate gene targets discovered by, or proprietary to, such companies. Antisense drug candidates are designed to bind to RNA targets through hybridization, and decrease production of the specific protein encoded by the target RNA. We believe that drugs based on antisense technology may be more effective and cause fewer side effects than conventional drugs in applications with well-defined RNA targets because antisense drugs are designed to intervene in a highly specific fashion in the production of proteins, rather than after the proteins are made.

We have licensed our rights related to antisense technology to certain parties. We also have in-licensed certain rights related to antisense technology.

*Out-licenses.* In 2001 we entered into an agreement with Isis Pharmaceuticals, Inc., under which we granted Isis a license, with the right to sublicense, to our antisense chemistry and delivery patents and patent applications; and we retained the right to use these patents and applications in our own drug discovery and development efforts and in collaborations with third parties. Isis paid us $15.0 million in cash and issued 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million and is required to pay us a mid double-digit percentage of specified sublicense income it receives from some types of sublicenses of our patents and patent applications. To date, we have received $0.3 million in sublicense income from Isis. Also under the agreement, we licensed from Isis specified antisense patents and patent applications, principally Isis suite of RNase H patents and patent applications. We also paid to Isis $0.7 million and issued 1,005,499 shares of common stock having a fair market value of app