IDERA PHARMACEUTICALS, INC.
Form 10-K
March 30, 2007

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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, 2006
OR
o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number: 001-31918

IDERA PHARMACEUTICALS, INC.
(Exact name of Registrant as specified in its certificate of incorporation)

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

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

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

Common Stock, $.001 par value
(Including Associated Preferred Stock Purchase Rights)
(Title of Class)

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 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. o

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

Large accelerated filer o Accelerated filer o Non-accelerated filer þ

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 $53,962,564 based on the last sale price of the registrant s common stock on the American Stock Exchange on June 30, 2006. As of March 13, 2007, the registrant had 21,204,797 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 on June 13, 2007 are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Form 10-K.

IDERA PHARMACEUTICALS, INC.

FORM 10-K

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FORWARD-LOOKING STATEMENTS

This annual report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements, other than statements of historical facts, 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, pro and would and similar 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 Item 1A Risk Factors. These factors and the other cautionary statements made in this annual report should be read as being applicable to all related forward-looking statements whenever they appear in this annual report. In addition, any forward-looking statements represent our estimates only as of the date that this annual report 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.

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PART I.

Item 1. *Business*

Overview

We are engaged in the discovery and development of synthetic DNA- and RNA-based compounds for the treatment of cancer, infectious diseases, autoimmune diseases, and asthma/allergies, and for use as vaccine adjuvants. We have designed proprietary product candidates to modulate immune responses through Toll-like Receptors, or TLRs. TLRs are specific receptors present in immune system cells that direct the immune system to respond to potential disease threats. Relying on our expertise in DNA and RNA chemistry, we are identifying product candidates targeted to TLRs 7, 8 or 9 for our internal development programs and for collaborative alliances. We are developing both agonists and antagonists of TLRs 7, 8 and 9. A TLR agonist is a compound that stimulates immune response through the targeted TLR. A TLR antagonist is a compound that blocks activation of an immune response through the targeted TLR. We have three internal programs, in oncology, infectious diseases, and autoimmune diseases, and two collaborative alliances relating to the development of treatments for asthma and allergies and the development of adjuvants for vaccines.

Our most advanced product candidate, IMO-2055, is an agonist of TLR9. We are currently conducting a Phase 2 trial of IMO-2055 in oncology and a Phase 1/2 trial of IMO-2055 in combination with chemotherapy in oncology. We have selected a second TLR9 agonist, IMO-2125, as a lead product candidate for treating infectious diseases and plan to submit an Investigational New Drug application, or IND, to the U.S. Food and Drug Administration, or FDA, for IMO-2125 in the second quarter of 2007. In our autoimmune disease program, which is in an earlier stage of research, we are evaluating TLR antagonists in preclinical models. We are collaborating with Novartis International Pharmaceutical, Ltd., or Novartis, for the discovery, development, and potential commercialization of TLR9 agonists for the treatment of asthma/allergy indications. We also are collaborating with Merck & Co., Inc., or Merck, for the use of our TLR7, 8 and 9 agonists in combination with Merck s therapeutic and prophylactic vaccines in the areas of oncology, infectious diseases, and Alzheimer s disease.

In October 2004, we commenced patient recruitment for an open label, multi-center Phase 2 clinical trial of IMO-2055 as a monotherapy in patients with metastatic or recurrent clear cell renal cancer. Under the protocol for the trial, we are seeking to enroll a total of up to 92 patients in the first stage of the trial, 46 who have failed one prior therapy and 46 who have not received any prior therapy. As of March 1, 2007, we had enrolled 43 patients who have failed one prior therapy and 45 patients who have not received any prior therapy. In October 2005, we initiated an open-label, single center Phase 1/2 clinical trial of IMO-2055 in combination with the chemotherapy agents gemcitabine and carboplatin in patients with refractory solid tumors. Under the protocol, we are seeking to enroll up to 26 patients in the Phase 1 portion of the trial to evaluate the safety of the combination. As of March 1, 2007, we had enrolled 18 patients in this trial. In July 2006, we formed an Oncology Clinical Advisory Board to advise us on the clinical development of IMO-2055 in oncology. We expect that we will commence additional clinical trials in 2007 to evaluate IMO-2055 in combinations with approved anticancer agents.

IMO-2125 is our second product candidate and also is an agonist of TLR9. In preclinical models, including cultures of human immune cells and nonhuman primates, IMO-2125 has induced high levels of interferon-alpha and other cytokines. In cell-based assays, these cytokines have shown potent activity in blocking replication of hepatitis C virus. Cytokines are proteins that initiate and modify immune responses. Interferon-alpha is a particularly important type of cytokine in that it controls the production of many factors that act directly on the immune system. We have carried out preclinical evaluations of IMO-2125 to support the submission of an IND, with the first targeted clinical indication

being hepatitis C. We expect to submit the IND to the FDA in the second quarter of 2007.

We have also identified DNA-based compounds that act as antagonists of TLRs 7, 8 and 9. We have carried out 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. We are conducting further preclinical studies to explore the potential of these novel compounds in autoimmune diseases.

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In May 2005, we entered into a research collaboration and option agreement and a license, development, and commercialization agreement with Novartis to discover, develop, and potentially commercialize TLR9 agonists that are identified as potential treatments for asthma and allergies. In February 2007, Novartis extended the initial two-year research collaboration by an additional year until May 2008.

In December 2006, we entered into an exclusive license and research collaboration agreement with Merck to research, develop and commercialize vaccine products containing our TLR7, 8 or 9 agonists in the fields of oncology, infectious diseases and Alzheimer s disease. Under the agreement, we have agreed to engage in a two-year research collaboration to generate novel agonists targeting TLR7 and TLR8, which may incorporate both Merck and Idera chemistry, for use in Merck s vaccines for oncology, infectious diseases and Alzheimer s disease.

At the close of business on June 29, 2006, we effected a one-for-eight reverse stock split of our issued and outstanding common stock. As a result of the reverse stock split, each share of common stock outstanding at the close of business on June 29, 2006 automatically converted into one-eighth of one share of common stock. All share and per share information in this annual report on Form 10-K reflects this reverse stock split.

Our Business Strategy

We believe that our compounds targeted to TLRs have broad potential applications in oncology, infectious diseases, autoimmune diseases, and asthma/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 seek to advance other applications through collaborations with pharmaceutical companies.

We have entered into collaborative relationships for application of our technology in two therapeutic areas. We believe that our collaborations with Novartis for asthma/allergies and Merck for vaccines provide the necessary resources and expertise to advance these complex research programs. These collaborations have also brought us upfront payments that have helped to finance our internal pipeline. These collaborations could also result in our receiving additional payments if agreed upon milestones are achieved. We may also receive royalties if any commercial products result from our collaborations. To obtain additional development resources and expertise, we may seek additional collaborations. As our internal program with IMO-2055 progresses in oncology, IMO-2125 advances in infectious disease, and the preclinical program moves forward in autoimmune diseases, we may continue to seek additional collaborations that will enable us to apply the resources needed to advance our internal programs.

We plan to stay at the forefront of TLR-based research and discovery by continuing to develop novel and proprietary DNA-and RNA-based compounds targeted to TLRs. We use these compounds, which are synthetic chemical structures, to populate our growing internal pipeline and to support our collaborative programs.

Overview of the Human Immune System

The immune system protects the body by working through various mechanisms to recognize and eliminate viruses, bacteria and other infectious agents, referred to as pathogens, and abnormal cells, such as cancer cells. These mechanisms initiate a series of interactions resulting in stimulation of specific genes 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 pathogenic invasion or to the presence of abnormal cells in the body and to activate the adaptive immune system. The innate immune system consists of cells such as macrophages, dendritic cells and monocytes. When the body is presented with a pathogen,

cells of the innate immune system are activated, 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.

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In contrast to the innate immune system, the adaptive immune system provides a pathogen-specific response to a pathogenic invasion. 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. This process is initiated through signals produced by the innate immune system. Upon recognition of a foreign 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 infected cells. 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 activated by a specific antigen, the adaptive immune system remembers the antigen. In this manner, if the pathogen again invades the body, the presence of the memory immunity will allow the adaptive immune system to respond once more, this time in a matter of days.

TLR-based Drug Discovery Technology

The human immune reaction is initiated by activation of the innate immune system. One way the activation of the immune system occurs is through recognition of a pathogen-associated molecular pattern, referred to as a PAMP. TLRs are a family of receptors that are known to recognize PAMPs. The different members of the TLR family of receptors are expressed in various immune system cells and recognize different PAMPs. Of the TLR receptors, TLR9 is a receptor that specifically recognizes bacterial DNA or 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 synthetic DNA- and RNA-based compounds, which as a chemical class are called oligonucleotides. Our compounds are developed to mimic the bacterial DNA and viral RNA that are recognized by TLR7, 8 or 9. We have designed some of our compounds to act as agonists of TLR7, 8 or 9 and other of our compounds to act as antagonists of TLR7, 8 and 9.

Our most advanced programs are directed at compounds that are agonists of TLR9. These compounds mimic bacterial DNA and induce immune responses through TLR9 that may be applicable to the treatment of cancer, infectious diseases and asthma and allergies, and to use as vaccine adjuvants. We have designed our TLR9 agonist candidates to stimulate the innate immune system to produce cytokines and other immune response activators. These cytokines and other activators lead to activation of the adaptive immune system. Furthermore, in preclinical cell culture and animal model studies, we have determined that the immunological activity of our compounds can differ depending on the structure of our compounds. The ability to change immunological activity through variations in chemical structure allows us to create a growing portfolio of compounds potentially useful for treating or preventing different diseases.

We are also designing synthetic RNA-based compounds that are agonists of TLRs 7 and 8. These RNA compounds are designed to mimic viral RNA. In preclinical studies in cell culture and animal models, these compounds induced immune responses. We believe that these responses may be applicable to the treatment of cancer and infectious diseases, as well as to use as vaccine adjuvants.

We also are developing new classes of compounds that are antagonists of TLRs 7, 8 and 9. In cell-based experiments and animal models, these antagonists have blocked immune reactions to specific agonists of TLR9 and specific agonists of TLRs 7 and 8. Recent preclinical studies from third-party researchers have suggested TLRs 7 and 9 play a role in certain autoimmune diseases, including lupus. We have evaluated some of our antagonist compounds in preclinical mouse models of lupus and have seen improvement in a number of disease parameters.

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Research and Development Programs

We and our collaborators are engaged in the evaluation of TLR-targeted compounds in several therapeutic areas. The following table summarizes the disease areas for which we and our collaborators are developing compounds and the status of these efforts.

Disease Area	Product candidate	Therapeutic Use	Development Status
		INTERNAL PROGRAMS	
Oncology	IMO-2055 IMO-2055 (in combination with chemotherapy agents)	Renal Cell Cancer Cancer solid tumors	Phase 2 Phase 1/2
Infectious Diseases	IMO-2125	Hepatitis C	Plan to Submit IND 2nd Quarter of 2007
Autoimmune Diseases	TLR Antagonist Candidates	Lupus	Research
		PROGRAMS UNDER COLLABORATION	
Respiratory Diseases	TLR9 Agonist Candidates	Asthma/Allergies	Being developed with Novartis
Vaccines for Cancer, Infectious Diseases, Alzheimer s Disease	TLR7, 8, 9 Agonist Candidates	Vaccine Adjuvants	Being developed with Merck

Our Development Programs

Oncology

Overview

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 is notoriously weak or absent. Various mechanisms to increase immune response to cancer cells have been evaluated by others, including bacterial extracts, *ex vivo* or *in vivo* stimulation of immune cells, and administration of recombinant cytokines such as interferons.

We believe that TLR9 agonists can enhance the body s immune response to cancer cells. We and others have conducted preclinical studies in human cell-based assays in which TLR9 agonists have activated cells of the immune system and induced these cells to secrete cytokines. In mouse models of cancer, we have shown that our TLR9 agonists induced an immune response that resulted in antitumor activity. The cascade of immune responses initiated by TLR9 agonists in these studies in mouse models also activated the adaptive immune system functions, and enhanced the recognition of antigens unique to the tumor, which are referred to as tumor-associated antigens.

In preclinical studies of some of our TLR9 agonists, enhanced recognition of tumor-associated antigens promoted production of specific antibodies and sensitized immune cells, both of which contribute to a memory immune response. When our TLR9 agonists were combined in preclinical mouse models with approved anticancer agents, including chemotherapies, antibodies, and newer biologically targeted agents such as inhibitors of proteins involved in

cancer cell growth and blood vessel formation, the observed anticancer activity was enhanced beyond that of the anticancer agents alone. We believe that TLR9 agonists also can be combined with tumor-associated antigens to enhance the immune responses to potential cancer vaccine candidates.

IMO-2055

IMO-2055, a synthetic DNA-based compound that is a TLR9 agonist, is our most advanced clinical product candidate. We selected IMO-2055 for clinical development because of the potency it demonstrated as an immune modulator in preclinical models, both *in vitro* and *in vivo*, and its activity in mouse models of cancer, both as a monotherapy and when combined with chemotherapies, antibodies, and newer biologically targeted agents, such as inhibitors of proteins involved in cancer cell growth and blood vessel formation. We filed an IND application for

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IMO-2055 with the FDA that became effective in March 2003. We have completed two Phase 1 clinical trials, have two ongoing clinical trials of IMO-2055 and plan to commence additional trials in 2007.

Healthy Volunteer Phase 1. In March 2004, we completed a Phase 1 clinical trial of IMO-2055 in 28 healthy volunteers over a range of dosing levels from 0.005 to 0.16 mg/kg/week for 3 weeks, by subcutaneous injection or intravenous infusion. In this single- center trial, IMO-2055 was well tolerated by the volunteers, who did not experience any significant treatment-related adverse effects. In addition, IMO-2055 demonstrated biological activity in the volunteers.

Refractory Solid Tumors Phase 1. In February 2006, we completed a Phase 1 clinical trial of IMO-2055 in 23 patients with refractory solid tumor cancers at the Lombardi Comprehensive Cancer Center at Georgetown University Medical Center in Washington, D.C. In the trial, we administered IMO-2055 to the patients by subcutaneous injection in weekly doses that ranged from 0.04 mg/kg/week to 0.64 mg/kg/week. IMO-2055 was administered to the patients weekly for a period of up to 104 weeks. IMO-2055 treatment exhibited evidence of immunological activity as measured by several laboratory tests of immune system function. IMO-2055 was well tolerated at all dosage levels. Adverse events experienced by patients were consistent with the expected immune stimulation activity of IMO-2055, and primarily were mild to moderate injection site reactions and flu-like symptoms including rigors/chills, fever, nausea, myalgia, headache, malaise and fatigue. Serious adverse events possibly related to IMO-2055 treatment included one patient with transient shortness of breath, one patient with rigors/chills, one patient with abdominal pain with nausea/vomiting, and two patients with anemia requiring transfusion. One patient received IMO-2055 therapy in the trial for 104 weeks and exhibited no serious adverse effects during the treatment period. The Phase 1 trial was conducted in patients with a variety of cancer types, including renal cell cancer, melanoma, colorectal cancer, sarcoma, breast cancer, non-small cell lung cancer, and others. Results from this trial were presented at the TOLL2004 meeting in Taormina, Italy in May 2004 and the American Society of Clinical Oncology, or ASCO, annual meeting in May 2005.

Renal Cell Cancer Phase 2. We are currently conducting a Phase 2 clinical trial of IMO-2055 in patients with metastatic or recurrent clear cell renal cancer. The trial, for which we began patient recruitment in October 2004, is a two-stage, multi-center, open label study of IMO-2055 as a monotherapy. In the trial, patients receive one of two dose levels, 0.16 or 0.64 mg/kg, by subcutaneous injection once a week for a period of up to 24 weeks if there continues to be an absence of disease progression. Patients can continue to receive IMO-2055 treatment beyond this 24-week period based on investigator recommendations and independent medical monitor concurrence. The primary objective of the study is to determine tumor response by Response Evaluation Criteria in Solid Tumors, or RECIST. Secondary study objectives include safety, duration of response, time to progression, survival one year after the last dose and the treatment effect on quality of life.

In this Phase 2 trial, we originally planned to recruit a minimum of 46 patients who had failed one prior therapy, which we refer to as second-line patients. The protocol also allowed for the enrollment of treatment-naïve patients, without specifying a target enrollment for treatment-naïve patients. In October 2005, in response to a higher than expected enrollment rate of treatment-naïve patients in the Phase 2 trial, we submitted to the FDA a protocol amendment that provided for enrollment of up to 46 treatment-naïve patients in the trial, in addition to the 46 second-line patients provided for by the original study design. As a result, we are now seeking to enroll a total of up to 92 patients in the trial. As of March 1, 2007, we had enrolled 88 patients in the trial, including 43 second-line patients and 45 treatment-naïve patients. In November 2006, we further amended the protocol to allow us to study additional immune system parameters in the trial.

Since this trial began in October 2004, two new drugs developed by other companies received FDA approval for the treatment of renal cell cancer. Nexavar® was approved in December 2005 and Sutent® was approved in January 2006. These drugs are now used extensively for the treatment of renal cell cancer, largely replacing the cytokine therapies,

interleukin-2 and interferon-alpha, which therapies were the standard of care for the treatment of renal cell cancer at the time we designed this trial. Our protocol excludes patients who have received more than one prior therapy, and the widespread use of these two new drugs has significantly slowed the enrollment rate in our phase 2 trial. As a result, we may not be able to complete enrollment of this trial. We will not be able to obtain a complete set of data from the trial until such time as no patients are continuing to receive treatment in the trial.

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This trial was initially designed as the first stage of a two-stage trial. Once we review the final data from the first stage, we will determine our next steps in the development of IMO-2055 for renal cell cancer, including whether to conduct the second stage of the trial or conduct a new trial. Because our phase 2 trial was designed on the basis of a potential alternative to interleukin 2 and interferon-alpha, we may determine not to continue development of IMO-2055 as monotherapy for renal cell cancer and instead may consider combination therapy trials with the approved drugs.

Refractory Solid Tumor Phase 1/2. We are currently conducting a Phase 1/2 clinical trial of IMO-2055 in combination with the chemotherapy agents gemcitabine and carboplatin in patients with refractory solid tumors. The trial, for which we began patient recruitment in October 2005, is a single center, open label safety study. We are seeking to enroll up to 26 refractory solid tumor patients in the Phase 1 portion of the trial to evaluate the safety of the combination. As of March 1, 2007, we had enrolled 18 patients in the trial and we expect to complete enrollment in the second quarter of 2007. In May 2006, we amended the protocol to investigate two additional treatment schedules of IMO-2055 administration in order to evaluate patient response to the 3-way combination.

Once we review the final data from Phase 1 of the trial, we plan to determine whether to conduct Phase 2 of the trial or conduct a new trial. We expect to announce the results of Phase 1 of this study by the end of 2007.

Future Clinical Development. In July 2006, we formed an Oncology Clinical Advisory Board, or OCAB, of ten internationally prominent physicians and scientists with broad expertise in oncology drug development and clinical practice to advise us on the clinical development of IMO-2055 in oncology, including which indications to pursue and trial design. Based on preclinical data, our clinical experience, and input from members of the OCAB, we plan to initiate new oncology clinical trials in 2007 to evaluate IMO-2055 in combination with standard approved oncology therapies in indications to be determined.

Infectious Diseases

Hepatitis C

Products composed of a single interferon protein, manufactured from a single gene, currently are part of the standard of care for the treatment of hepatitis C chronic infection. Natural interferon produced by the body as part of an immune response is a family of many proteins derived from multiple genes. We and others have shown in preclinical studies and in clinical trials that agonists of TLR9 stimulate the production of various cytokines, including the natural forms of interferon and other antiviral cytokines. The immune responses induced by TLRs also lead to development of adaptive immune responses, due to activation of antigen-presenting cells and generation of sensitized immune cells. Because of the activity generated by natural interferons induced through TLR9, we believe TLR agonists could provide potential advantages over manufactured interferon for the treatment of hepatitis C virus infection.

IMO-2125

We have selected IMO-2125, a TLR9 agonist, as our lead candidate for the treatment of hepatitis C virus infection. In preclinical models, including cultures of human immune cells and in nonhuman primates, IMO-2125 has been shown to induce high levels of natural interferons and other cytokines. The cytokines induced by IMO-2125 in human immune cell cultures and plasma from nonhuman primates dosed with IMO-2125 have shown potent activity in inhibition of hepatitis C virus RNA production in cell-based assays. We have completed various preclinical assessments of IMO-2125 with the plan to submit an IND in the second quarter of 2007 with an initial indication of treatment of hepatitis C virus infection.

Autoimmune Diseases

In autoimmune diseases such as lupus, the immune system mistakenly forms antibodies to a molecule that is correctly part of the body, also known as a self-antigen. An immune complex is then formed between the self-antigen and the antibody to the self-antigen. Recently, third-party researchers have reported that TLRs 7 and 9 may recognize these immune complexes and induce further immune response to them. In such a disease state, blocking

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immune responses that are mediated through TLR7 or TLR9 may interfere with the pathogenesis of the disease by reducing recognition of the immune complex.

We have identified DNA-based compounds that act as antagonists of TLRs 7, 8, and 9 and block immune responses mediated through these TLRs. We believe that such antagonists may have potential application in 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. Data from evaluation of our antagonist candidates in the mouse models showed improvement in a number of lupus disease parameters, including protection from the development of skin rash, decreases in the self-antigen antibodies, and reduced disease-related changes in the kidneys. We plan to conduct further preclinical studies to explore the potential of these novel DNA-based compounds for the treatment of autoimmune diseases.

Asthma and Allergies

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 designed to suppress symptoms of allergic or asthmatic response. TLR9 agonists, on the other hand, are designed to induce immune responses that could be useful in restoring immune system balance. In preclinical studies, our TLR9 agonists have shown improvements in multiple indices of allergic conditions. For example, in animal models of allergy, our TLR9 agonists were shown to restore the balance of immunological activity, produce a higher ratio of specific versus non-specific antibodies, reduce the number of pulmonary immune cells that produce allergic inflammation, and improve lung function.

We have entered into a research collaboration and option agreement and a separate license, development, and commercialization agreement with Novartis to discover, optimize, develop, and potentially commercialize TLR9 agonists that are identified as potential treatments for asthma and allergies.

Vaccine Adjuvants

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

We have entered into a research collaboration with Merck and have granted Merck a worldwide, exclusive license to develop and commercialize our TLR7, 8, and 9 agonists by incorporating them in therapeutic and prophylactic vaccines being developed by Merck for oncology, infectious diseases, and Alzheimer s disease.

We have granted a non-exclusive license for a TLR9 agonist to The Immune Response Corporation to research, develop, and commercialize the potential application of IMO-2055 for use in its development of one specific potential therapeutic and prophylactic HIV vaccine. The Immune Response Corporation is currently conducting Phase 1 clinical trials of this product.

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Corporate 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.

Novartis International Pharmaceutical, Ltd.

In May 2005, we entered into a research collaboration and option agreement and a separate license, development and commercialization agreement with Novartis to discover, develop and potentially commercialize TLR9 agonists that are identified as potential treatments for asthma and allergies. In addition, beginning on May 31, 2007, if specified conditions are satisfied, Novartis may expand the collaboration to include additional human disease areas, other than oncology and infectious diseases.

The agreements with Novartis are structured in two phases. During the research collaboration phase, we and Novartis have agreed to work together to evaluate novel TLR9 agonists from which Novartis may select one or more product candidates for further development through human clinical proof of concept trials. Based on the results of the research collaboration, Novartis may then elect to implement the commercialization agreement, and, under the license, development and commercialization agreement, complete the development, and commercialize one or more of the product candidates.

Under the terms of the agreements:

- Upon execution of the agreements, Novartis paid us a $4.0 million upfront license fee;
- Novartis agreed to fund substantially all research activities during the research collaboration phase;
- If Novartis elects to exercise its option to develop and commercialize licensed TLR9 agonists in the initial collaboration disease areas, Novartis is potentially obligated to pay us up to $131.0 million based on the achievement of clinical development, regulatory approval, and annual net sales milestones;
- Novartis is potentially obligated to pay us additional milestone payments if Novartis elects to expand the collaboration to include additional disease areas and then develops and commercializes licensed TLR9 agonists in the additional disease areas based on the achievement of clinical development and regulatory approval milestones;
- Novartis is also obligated to pay us royalties on net sales of all products, if any, commercialized by Novartis, its affiliates and sublicensees; and
- Novartis license rights under the agreements to products that it elects to develop and commercialize are worldwide, exclusive rights.

We and Novartis agreed that the term of the research and collaboration phase would be two years commencing in May 2005. In February 2007, Novartis extended our research collaboration by an additional year until May 2008. In connection with this extension, Novartis will pay us an additional license fee of $1.0 million. Under the agreements, Novartis obligations to pay us royalties extend, on a product-by-product and country-by-country basis, until the expiration of the patent rights covering the product licensed to Novartis in countries in which there is coverage by licensed patent rights, and, in countries in which there is no coverage by licensed patent rights, until the earlier of the

last day of the calendar year in which Novartis loses market exclusivity with respect to a product and the date 10 years after the product s commercial launch.

Novartis may terminate the research collaboration and option agreement without cause upon 90 days written notice to us and the license, development, and commercialization agreement upon 60 days written notice to us. Upon 30 days written notice, either party may terminate the research collaboration and option agreement for a material breach if such breach is not cured within the 30-day notice period, and upon 90 days written notice, either party may terminate the license, development, and commercialization agreement if such breach is not cured within the 90-day notice period. Upon 30 days written notice, either party may terminate the research collaboration and option agreement and/or the license, development, and commercialization agreement upon the other party s filing of bankruptcy.

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Merck & Co., Inc.

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

Merck paid us a $20.0 million upfront license fee;

Merck purchased $10.0 million of our common stock at $5.50 per share;

Merck agreed to fund the research and development collaboration;

Merck 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 develops and commercializes additional vaccines using our agonists, we would be entitled to receive additional milestone payments and

Merck agreed to pay us royalties on net product sales of vaccines using our TLR agonist technology that are developed and marketed.

Merck has agreed, subject to certain exceptions, that prior to December 8, 2007, it will not sell any of the shares of our common stock acquired by it under the agreement and that, for the duration of the research and collaboration term, its ability to sell such shares will be subject to specified volume limitations.

Under the agreement, Merck 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 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 shall continue to pay us royalties at a reduced royalty rate until such anniversary, except that Merck 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 vaccine. In addition, the applicable royalties may be reduced if Merck is required to pay royalties to third parties for licenses to intellectual property rights, which royalties exceed a specified threshold. Merck s royalty and milestone obligations may also be reduced if Merck terminates the agreement based on specified uncured material breaches by us.

Merck may terminate the collaboration relationship 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 collaboration relationship 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.

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TLR Licenses

We have granted a non-exclusive license to The Immune Response Corporation to research, develop, and commercialize the potential application of IMO-2055 agonist for use as an adjuvant in one specific vaccine candidate for the treatment and prevention of HIV. Under the terms of the agreement, The Immune Response Corporation agreed to pay us royalties on its sales of licensed products and a percentage of sublicense income. Either party may terminate the license agreement for a material breach or a breach of a payment obligation, unless such breach is cured within the notice period.

Antisense Technology

We have been a pioneer in the development of antisense technology. Although we are no longer developing this technology, we believe that our antisense technology may be useful to pharmaceutical and biotechnology companies that are seeking to develop product candidates that down-regulate gene targets discovered by, or proprietary to, such companies. Antisense product candidates are designed to bind, through hybridization, RNA targets and modulate 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.

Currently, we are a party to five collaboration and license agreements involving the use of our antisense technology and specified indications. These agreements include a license agreement with Isis Pharmaceuticals, Inc. involving intellectual property for antisense chemistry and delivery.

Under the agreement with Isis, 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 an initial licensing fee and is required to pay us a portion of specified sublicense income it receives from some types of sublicenses of our patents and patent applications. 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 an initial licensing fee for this license and are obligated to pay Isis a maintenance fee and royalties. We have the right to use these patents and patent applications in our drug discovery and development efforts and in some types of third party collaborations. The licenses granted under the Isis agreement terminate upon the last to expire of the patents and patent applications licensed under the agreement. We may terminate at any time the sublicense by Isis to us of the patents and patent applications.

We are also a party to four other license agreements involving the license of our antisense patents and patent applications for specific gene targets under which we typically are entitled to receive license fees, sublicensing income, research payments, payments upon achievement of developmental milestones, and royalties on product sales. These agreements typically expire upon the later of the last to expire of the licensed patents or a specified number of years after the first commercial sale of a licensed product. These agreements may be terminated by either party for a material breach, and our collaborators may terminate these agreements at any time for convenience, with written notice.

We are also a party to six royalty-bearing license agreements under which we have acquired rights to antisense related patents, patent applications, and technology. Each of these in-licenses automatically terminates upon the expiration of the last to expire patent included in the license. Our principal in-license is with University of Massachusetts Medical Center for chemistry and for certain gene targets. Additionally, as part of a 2003 interference resolution for one of the

licensed patents, a settlement was made enabling us to receive a percentage of the royalty amounts the National Institutes of Health receives for the sale of a product that is covered by such patent. Under these in-licenses, we are obligated to pay royalties on our net sales of products or processes covered by a valid claim of a licensed patent or patent application. In certain cases, we are required to pay a specified percentage of any sublicense income, and all of these licenses impose various commercialization, sublicensing, insurance, and other obligations on us, and our failure to comply with these requirements could result in termination of the licenses.

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Research and Development Expenses

For the years ended December 31, 2006, 2005 and 2004, we spent approximately $12.7 million, $11.2 million and $8.2 million, respectively, on research and development activities. In 2005, Novartis sponsored approximately $1.0 million of our research and development activities. Our collaborators sponsored only a nominal portion of our research and development activities in 2006 and 2004.

Patents, Proprietary Rights and Trade Secrets

Patents and Proprietary Rights

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We use a variety of methods to seek to protect our proprietary position, including filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We have devoted and continue to devote a substantial amount of our resources into establishing intellectual property protection for:

Novel chemical entities that function as agonists of TLR7, 8 or 9;

Novel chemical entities that function as antagonists of TLR7, 8 and 9; and

Use of our novel chemical entities and chemical modifications to treat and/or prevent a variety of diseases.

As of February 28, 2007, we owned 49 U.S. patents and U.S. patent applications and 142 corresponding worldwide patents and patent applications for our TLR-targeted immune modulation technologies. These patents and patents applications include novel chemical compositions of matter and methods of use for our immunomodulatory compounds. Patent applications covering the compositions of matter and methods of use for IMO-2055 and IMO-2125 are pending worldwide.

To date, all of our intellectual property covering immune modulation compositions and methods of their use is based on discoveries made solely by us. The earliest of the issued patents for these discoveries expires in 2017.

In addition to our TLR-targeted patent portfolio, we are the owner or hold licenses of patents and patent applications related to antisense technology. As of February 28, 2007, our antisense patent portfolio included 112 U.S. patents and patent applications and 216 patents and patent applications throughout the rest of the world. These antisense patents and patent applications include novel compositions of matter, the use of these compositions for various genes, sequences and therapeutic targets, and oral and other routes of administration. Some of the patents and patent applications in our antisense portfolio were in-licensed. These patents expire at various dates ranging from 2007 to 2022.

Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in each of our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set

forth in these patent applications.

Litigation may be necessary to defend against or assert claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us, or to determine the scope and validity of the proprietary rights of others. In addition, the U.S. Patent and Trademark Office may declare interference proceedings to determine the priority of inventions with respect to our patent applications or reexamination or reissue proceedings to determine if the scope of a patent should be narrowed. Litigation or any of these other proceedings could result in substantial costs to and diversion of effort by us, and could have a material adverse effect on our business, financial condition and results of operations. These efforts by us may not be successful.

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Trade Secrets and Confidentiality Agreements

We may rely, in some circumstances, on trade secrets and confidentiality agreements to protect our technology. Although trade secrets are difficult to protect, wherever possible, we use confidential disclosure agreements to protect the proprietary nature of our technology. We regularly implement confidentiality agreements with our employees, consultants, scientific advisors, and other contractors and collaborators. However, there can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets and/or proprietary information will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Government Regulation

The testing, manufacturing, labeling, advertising, promotion, distribution, import, export, and marketing, among other things, of drugs are extensively regulated by governmental authorities in the United States and other countries. In the U.S., the FDA regulates pharmaceutical products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and other laws and regulations. Both before and after approval for marketing is obtained, violations of regulatory requirements may result in various adverse consequences, including the FDA s delay in approving or refusal to approve a drug, withdrawal of approval, suspension or withdrawal of an approved product from the market, operating restrictions, warning letters, product recalls, product seizures, injunctions, fines, and the imposition of civil or criminal penalties.

The steps required before a product may be approved for marketing in the U.S. generally include: