IDERA PHARMACEUTICALS, INC.
Form 10-K
March 11, 2008

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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, 2007
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.)**
167 Sidney Street Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(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 (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 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, 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 $112,169,323 based on the last sale price of the registrant s common stock as reported on the NASDAQ Global Market on June 30, 2007. As of February 29, 2008, the registrant had 21,987,744 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 4, 2008 are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Form 10-K.

IDERA PHARMACEUTICALS, INC.

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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 II, 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.

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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 diseases, cancer, and asthma and allergies, and for use as vaccine adjuvants. Drug candidates are compounds that we are developing and have not been approved for any commercial use. TLRs are specific receptors present in immune system cells that recognize the DNA or RNA of pathogens such as 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 compounds 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. Collaborations provide us with financial resources for our research and development programs and the necessary resources and drug development experience for our partnered programs.

We are focused on developing TLR-targeted compounds for the potential treatment of infectious diseases, autoimmune diseases, and cancer. IMO-2125, a TLR9 agonist, is our lead drug candidate for infectious diseases. At present, we are conducting a Phase 1 clinical trial of IMO-2125 in patients with chronic hepatitis C virus infection who have not responded to current standard of care therapy. The trial is designed to assess the safety of IMO-2125. In addition, the trial is designed to evaluate the effects of IMO-2125 on hepatitis C virus RNA levels and parameters of immune system activation.

As part of our infectious disease program, we are also evaluating RNA-based compounds that act as agonists of TLR7 and TLR8. We refer to our TLR7 and TLR8 agonists as **s**tabilized **i**mmune **m**odulatory **RNA**, or SIMRA, compounds. We have evaluated these compounds in preclinical studies in human cell-based assays and *in vivo* in non-human primates. We intend in 2008 to further evaluate these compounds in preclinical models of infectious disease.

In our autoimmune disease program we have identified DNA-based compounds that act as antagonists of TLR7 and TLR9. We have evaluated these compounds in various preclinical studies, including in mouse models of lupus and rheumatoid arthritis. We are currently conducting further preclinical studies to explore the potential of these compounds in multiple sclerosis and psoriasis.

Our cancer treatment research program is focused on potential applications of our TLR7 and TLR8 agonists. We intend in 2008 to evaluate these compounds in preclinical models of cancer.

We are also collaborating with three pharmaceutical companies to advance our TLR-targeted compounds in multiple disease areas. We are collaborating with Merck KGaA for cancer treatment excluding cancer vaccines, with Merck & Co., Inc., or Merck & Co., for vaccine adjuvants, and with Novartis International Pharmaceutical, Ltd., or Novartis, for treatment of asthma and allergies. Merck KGaA and Merck & Co. are not related.

In December 2007, we entered into a worldwide licensing and collaboration agreement with Merck KGaA for the research, development and commercialization of our TLR9 agonists for the treatment of cancer, excluding cancer vaccines. Under the agreement, we exclusively licensed our clinical stage drug candidates IMO-2055 and IMO-2125, as well as other TLR9 agonists, for the treatment of cancer, excluding cancer vaccines. We and Merck KGaA are evaluating IMO-2055 in clinical trials in cancer patients.

In December 2006, we entered into an exclusive license and research collaboration agreement with Merck & Co. to research, develop and commercialize therapeutic and prophylactic vaccine products containing our TLR7, 8 or 9 agonists in the fields of cancer, infectious diseases and Alzheimer s disease. Under the agreement, we are engaged in a two-year research collaboration to generate novel agonists targeting TLR7 and TLR8, which may

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incorporate both Merck & Co. and Idera chemistry, for use in Merck & Co. s vaccines for cancer, infectious diseases and Alzheimer s disease.

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 as potential treatments for asthma and allergies. In 2007, Novartis extended the initial two-year research collaboration by an additional year to May 2008. In March 2008, we agreed with Novartis to extend the research collaboration until December 31, 2008. The extension is anticipated to allow for the advancement of QAX935, a novel agonist of TLR9, into human clinical trials prior to the end of the research collaboration term.

Our Business Strategy

We believe that our compounds targeted to TLRs have broad potential applications in the treatment of infectious diseases, autoimmune 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 relationships for application of our technology in multiple therapeutic areas. We believe that our collaborations with Merck KGaA for cancer treatment excluding cancer vaccines, Merck & Co. for vaccine adjuvants, and Novartis for treatment of asthma and allergies provide the necessary resources and expertise to advance these programs. These collaborations have also brought us upfront payments that have helped to finance our research and development programs. These collaborations could also result in us receiving additional payments if agreed upon milestones are achieved. We may also receive royalties if any commercial products result from our collaborations.

As our clinical evaluation of IMO-2125 advances in chronic hepatitis C virus infection and our preclinical programs move forward in infectious diseases, autoimmune diseases, and cancer, we may continue to seek additional collaborations. 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 plan to stay at the forefront of TLR-based research and discovery by applying our chemistry-based approach to create and develop novel and proprietary DNA- and RNA-based compounds targeted to TLRs. We use these compounds, which are synthetic chemical structures, 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 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 specialized 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.

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

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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 invades the body, the presence of the memory immunity will allow the adaptive immune system to respond again, this time in a matter of days.

TLR-based Drug Discovery Technology

The human immune system is activated by recognition of pathogen-associated molecular patterns, or PAMPs. TLRs comprise 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 certain DNA patterns that occur in 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

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 infectious diseases, cancer, and asthma and allergies, and for use as vaccine adjuvants. We have created our TLR9 agonist candidates to activate specific cells of the immune system to 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 determined that the immunological activity of our compounds can be changed by modifying the structure of our compounds. Our ability to change immunological activity by modifying the chemical structure allows us to create a growing portfolio of compounds 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. These RNA-based compounds are designed to mimic viral RNA. In preclinical studies in cell culture and animal models, these compounds induced immune responses that we believe may be applicable to the treatment of cancer and infectious diseases and vaccine adjuvants.

TLR7 and TLR9 Antagonists

We are creating novel classes of compounds that are designed to be antagonists of TLR7 and TLR9. Recent preclinical studies from third-party researchers have suggested TLR7 and TLR9 may play a role in certain autoimmune diseases. In cell-based experiments and animal models, our antagonists have blocked immune stimulation in the presence of specific agonists of TLR9 and specific agonists of TLR7. We have evaluated some of our antagonist compounds in preclinical mouse models of the human autoimmune diseases lupus and rheumatoid arthritis. In both of these models, treatment with our antagonist compounds was associated with 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 multiple therapeutic areas. The following table summarizes the disease areas and the development status for our programs.

RESEARCH AND DEVELOPMENT PROGRAMS

Disease Area	Drug candidate(s)	Development Status
Infectious Diseases		
Chronic Hepatitis C	IMO-2125 (TLR9 agonist)	Phase 1 Clinical Trial
Viral Diseases	TLR7, 8 and 9 agonists	Research
Autoimmune Diseases		
Lupus, Rheumatoid Arthritis, Multiple Sclerosis, Psoriasis	TLR7, TLR9 antagonists	Research
Oncology		
Solid Tumor Cancers	TLR7, TLR8 agonists	Research

PARTNERED PROGRAMS

Disease Area	Drug candidate(s)	Development Status
Oncology: TLR9 agonists in collaboration with Merck KGaA		
Renal Cell Carcinoma	IMO-2055	Phase 2 Stage A Clinical Trial
Solid Tumors	IMO-2055 + Chemotherapy	Phase 1 Clinical Trial
Non-small Cell Lung Cancer	IMO-2055 in combination with Tarceva® and Avastin®	Phase 1b Clinical Trial
Colorectal Cancer	IMO-2055 in combination with Erbitux® and Camptosar®	Preclinical
Vaccines: TLR7, 8, 9 agonists in collaboration with Merck & Co.		
Cancer, Infectious Diseases, Alzheimer s Disease	TLR7, 8 and 9 agonists as vaccine adjuvants	Research
Respiratory Diseases: TLR9 agonists in collaboration with Novartis		
Asthma, Allergies	QAX935	Preclinical

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 that have potential therapeutic applicability in infectious diseases, including those caused by viruses.

Our most advanced application of TLR-targeted drug candidates in infectious diseases involves DNA-based compounds that mimic bacterial DNA and are recognized as agonists of TLR9. Certain TLR9 agonists induce high levels of interferon-alpha in preclinical models. Recombinant interferon products currently are components of the standard of care for viral infectious diseases such as chronic hepatitis C infection.

Hepatitis C IMO-2125

Currently, the standard of care treatment for chronic hepatitis C virus infection is based on therapies that include a single recombinant interferon protein. We and others have shown in preclinical studies TLR9 agonists induce many proteins, including natural interferon proteins and other proteins with antiviral activity. The induction of natural interferon and other antiviral proteins through TLR9 leads us to believe that TLR9 agonists may provide

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advantages over recombinant interferon for the treatment of chronic hepatitis C virus infection because the induced proteins may act in concert to produce a broader or stronger antiviral effect.

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

In May 2007, we submitted an investigational new drug, or IND, application for IMO-2125 to the FDA, and in September 2007, we initiated a Phase 1 study of IMO-2125 in patients with chronic hepatitis C virus infection who have not responded to the current standard of care treatment. We are currently recruiting patients at five sites and plan to enroll up to 40 patients in four cohorts at escalating IMO-2125 dose levels, with four weeks of treatment. Of the ten patients per cohort, eight will be randomized to receive IMO-2125 treatment and two will be randomized to receive placebo treatment. The trial is designed to assess the safety of IMO-2125 at each dose level. Secondary objectives include assessments of the effects of IMO-2125 on hepatitis C virus RNA levels and parameters of immune system activation. We anticipate interim results from this trial will be available in the first half of 2009.

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

Viral Diseases

We intend in 2008 to evaluate some of our compounds in preclinical models of viral infectious diseases other than chronic hepatitis C virus infection. In addition to our TLR9 agonists such as IMO-2125, we have identified synthetic RNA-based compounds that mimic viral RNA and are recognized by TLR7 and TLR8. We have discovered structural approaches that stabilize these compounds, which we call SIMRA structures. We have reported data from preclinical studies in human cell-based assays and *in vivo* in non-human primates in which our TLR7 and TLR8 agonist compounds induced immune responses that might be applicable to the treatment of viral infectious diseases.

Autoimmune Diseases

Systemic lupus erythematosus, or lupus, and rheumatoid arthritis are examples of chronic autoimmune diseases in which the immune system attacks the cells and tissues of the body and causes inflammation and tissue damage. Current therapies include corticosteroids and anti-malarial drugs such as chloroquine. In autoimmune diseases such as lupus and rheumatoid arthritis, the immune system forms antibodies to a molecule that is an appropriate 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 TLR7 and TLR9 may recognize these immune complexes and induce further immune responses to them.

We have identified DNA-based compounds that in preclinical studies have acted as antagonists of TLR7 and TLR9. In studies conducted in mouse models, these antagonists inhibited immune responses mediated through TLR7 and TLR9. We believe that such antagonists may have application in the treatment of autoimmune diseases because they may inhibit TLR7 or TLR9 mediated responses to the immune complex and thereby interfere with the progression of disease symptoms.

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 and in a

collagen-induced mouse model of rheumatoid arthritis. Data from these evaluations showed improvement in a number of disease parameters. We plan to conduct preclinical studies in additional models, including mouse models of multiple sclerosis and psoriasis, to explore the potential of these novel DNA-based compounds for the treatment of autoimmune diseases. In 2008, we intend to form a scientific advisory board with leading researchers in the field of autoimmune diseases to assist with determining a clinical development strategy for our antagonist candidates. We expect to select a lead antagonist candidate for a defined autoimmune disease and to initiate IND-enabling studies in 2008.

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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. Various mechanisms to increase the immune response to cancer cells have been evaluated by others, including the use of bacterial extracts, *ex vivo* or *in vivo* stimulation of immune cells, and administration of recombinant proteins such as interferons. We believe that agonists of TLRs 7, 8, and 9 can enhance the body s immune response to cancer cells.

We have identified synthetic SIMRA compounds that mimic viral RNA and are recognized by TLR7 and TLR8. We have reported data from preclinical studies in human cell-based assays and *in vivo* in non-human primates in which SIMRA compounds induced immune responses. In the reported data the agonistic activity for TLR7 and TLR8 was dependent on the chemical composition of the SIMRA compounds. We intend to further evaluate these compounds in preclinical cancer models.

We and other researchers have published and presented extensive data on our DNA-based agonists of TLR9 in mouse models of cancer. We have shown in these mouse models 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.

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 also believe that TLR9 agonists can be combined with tumor-associated antigens to enhance the immune responses to potential cancer vaccine candidates. In preclinical studies conducted by us 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 an adaptive immune response.

Partnered Programs

We selected IMO-2055, a synthetic DNA-based TLR9 agonist, as a lead candidate for the treatment of cancer. 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. Prior to entering our collaboration with Merck KGaA, we completed, initiated, or planned the following clinical studies with IMO-2055.

Healthy Volunteer Phase 1 Trial. In March 2004, we completed a Phase 1 clinical trial of IMO-2055 in 28 healthy volunteers over a range of dose 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 evidence of immune stimulatory activity in the volunteers.

Refractory Solid Tumor Monotherapy Phase 1 Trial. 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 this 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 for 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.

Renal Cell Cancer Monotherapy Phase 2 Stage A Trial. In October 2004, we commenced patient recruitment for an open label, multi-center Phase 2 Stage A 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 sought to enroll a total of up to 92 patients in Stage A of the trial, 46 who had failed one prior therapy and 46 who were treatment-naïve. We closed enrollment in this trial on June 29, 2007. As of that date, we had enrolled 46 treatment-naïve patients and 45 patients who had failed one prior therapy. We will be able to obtain a complete set of data only when all patients have stopped receiving treatment in the trial. As of March 2008, one patient continued to receive treatment in the trial. We expect that initial data from this trial will be available in the second or third quarter of 2008.

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Refractory Solid Tumor Chemotherapy Combination Phase 1 Trial. In October 2005, we began patient recruitment in the Phase 1 portion of a clinical trial of IMO-2055 in combination with the chemotherapy agents gemcitabine and carboplatin in patients with refractory solid tumor cancers. The purpose of the Phase 1 portion of the trial, which was a single center, open label study, was to evaluate the safety of the chemotherapy combination. Three dose levels of IMO-2055 and three treatment schedules of IMO-2055 were investigated in this trial. We enrolled twenty-two patients in this trial and closed enrollment in July 2007. We reported interim data from 19 patients from this trial at the 12th World Conference on Lung Cancer in Seoul, Korea, in September 2007. The interim data suggested that it was feasible for the combination of IMO-2055, gemcitabine, and carboplatin to be administered in patients with advanced solid tumors. The only dose-limiting toxicities observed in these patients were common side effects observed with gemcitabine and carboplatin. In these 19 patients, the response rate, progression-free survival, and overall survival were 5%, 4.1 months, and 12.9 months, respectively. In the subset of eight patients with non-small cell lung cancer, the response rate, progression-free survival, and overall survival were 13%, 6.5 months and 12.9 months, respectively.

Non-small Cell Lung Cancer Avastin® and Tarceva® Combination Phase 1b Trial. In December 2007, we initiated a Phase 1b trial of IMO-2055 in combination with Avastin and Tarceva in non-small cell lung cancer patients whose cancer had progressed during a prior course of standard therapy. The trial is designed to assess safety of the IMO-2055, Tarceva and Avastin combination and to determine the recommended dosage of IMO-2055 for potential use in a subsequent Phase 2 trial. Three dose levels of IMO-2055 are being investigated with standard dosages and schedules of Tarceva and Avastin. IMO-2055 is administered 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 is met. We are currently recruiting patients for the trial, which was designed with a target enrollment of up to 40 patients.

Colorectal Cancer Erbitux® and Camptosar® Combination Phase 1b Trial. In 2007, we made plans to initiate a clinical trial in the U.S. to investigate IMO-2055 in combination with Erbitux, a recombinant, humanized antibody to epidermal growth factor receptor, and Camptosar, a cytotoxic, chemotherapeutic agent that inhibits topoisomerase I function, in patients with colorectal cancer. The Phase 1b trial is designed to evaluate multiple dose levels of IMO-2055 with established treatment regimens for Erbitux and Camptosar.

We have agreed with Merck KGaA that we will complete the Phase 2 renal cell cancer trial and the Phase 1 refractory solid tumor chemotherapy combination trial. We also have agreed with Merck KGaA that we will continue to conduct on its behalf the on-going Phase 1b non-small cell lung cancer trial and that we may initiate the proposed Phase 1b colorectal cancer trial. Merck KGaA has agreed to reimburse us for the development costs associated with these two Phase 1b clinical trials incurred after February 4, 2008, which is the date our agreement with Merck KGaA became effective.

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 shown adjuvant activity when combined 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 & Co. and have 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.

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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 generally designed to suppress symptoms of asthmatic or allergic 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 conducted by us and our collaborators, our TLR9 agonists have shown improvements in multiple indices of allergic conditions. For example, we have presented data from mouse models of allergy which show 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.

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. In March 2008, we agreed with Novartis to extend the research collaboration until December 31, 2008. The extension is anticipated to allow for the advancement of QAX935, a novel agonist of TLR9, into human clinical trials prior to the end of the research collaboration term.

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.

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/or 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 will continue to be conducted by us;
- 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 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/or delaying of the onset or progression of cancer in humans; and

Develop or commercialize IMO-2055 for use outside treating, curing and/or delaying of 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 Idera is pursuing under its collaboration with Merck & Co.

These restrictions will not limit Idera s 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.

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During the period in which we provide follow-on TLR9 agonists, we agreed to form a joint research committee, consisting of an equal number of members from Idera and Merck KGaA, to facilitate our delivery of such compounds.

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 shall continue to pay us royalties 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.

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, which collaboration may be extended by Merck & Co. for two additional one-year periods. 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 royalties on net product sales of vaccines using our TLR agonist technology that are developed and marketed.

Merck & Co. agreed, subject to certain exceptions, that prior to December 8, 2007, it would 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 & 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. shall continue to pay us royalties at a reduced royalty rate until such anniversary, except that

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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 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.

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, Novartis may expand the collaboration, if specified conditions are satisfied, to include additional disease areas, excluding oncology and infectious diseases.

The agreements with Novartis are structured in two phases. During the research collaboration phase, we and Novartis agreed to work together to evaluate novel TLR9 agonists from which Novartis may select one or more drug candidates for further development through human clinical trials. In March 2008, we agreed with Novartis to extend the research collaboration until December 31, 2008. The extension is anticipated to allow for the advancement of QAX935, a novel agonist of TLR9, into human clinical trials prior to the end of the research collaboration term. Based on the results of the research collaboration, Novartis may elect to implement the commercialization agreement, and, under the license, development and commercialization agreement, complete the development and commercialize one or more of the drug 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 2007, Novartis extended our research collaboration by an additional year to May 2008. In connection with this extension, Novartis paid us an additional license fee of $1.0 million. In 2008, we agreed to extend the research collaboration until December 31, 2008.

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

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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.

Antisense Technology

We have been a pioneer in the development of antisense technology. Although we are not actively developing this technology at present, we 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.

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., or Isis, 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.

In 2007, we gave formal notice to Isis that we believed that Isis had materially breached certain provisions of the Collaboration and License Agreement, or the Collaboration Agreement, between us and Isis dated May 24, 2001. We and Isis submitted the dispute to arbitration and in January 2008, the arbitrator decided that Isis had not breached the Collaboration Agreement. The results of this arbitration are not material to us and have not changed the rights we reserved in the Collaboration Agreement to practice our intellectual property.

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

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Massachusetts Medical Center for chemistry and for certain gene targets. Under all of 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. 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.

Research and Development Expenses

For the years ended December 31, 2007, 2006 and 2005, we spent approximately $13.2 million, $12.7 million and $11.2 million, respectively, on research and development activities. In 2007, Merck & Co. sponsored approximately $1.1 million of our research and development activities. Our collaborators sponsored only a nominal portion of our research and development activities in 2006. In 2005, Novartis sponsored approximately $1.0 million of our research and development activities.

Patents, Proprietary Rights and Trade Secrets

Our success depends in part on our ability to obtain and maintain proprietary protection for our drug 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 or 9; and

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

As of February 29, 2008, we owned 61 U.S. patents and U.S. patent applications and 161 corresponding worldwide patents and patent applications for our TLR-targeted immune modulation technologies. These patents and patent applications include novel chemical compositions of matter and methods of use for our immune modulatory compounds, including IMO-2055 and IMO-2125.

To date, all of our intellectual property covering immune modulatory 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. The U.S. patent specifically covering the composition of IMO-2055 expires in 2023.

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 29, 2008, our antisense patent portfolio included 103 U.S. patents and patent applications and 159 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 2014 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.

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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.

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:

- nonclinical laboratory tests and animal tests under the FDA s good laboratory practices regulations;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for each indication;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is made to assess compliance with the FDA s regulations on current good manufacturing practices, or cGMPs; and
- the submission to the FDA of an new drug application, or NDA, or a biologic license application, or BLA.

Nonclinical tests include laboratory evaluation of the product, as well as animal studies to assess the potential safety and pharmacological activity of a drug. The results of the nonclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may be commenced. The IND will automatically become effective 30 days after its receipt by the FDA, unless the FDA before that time raises concerns or questions about the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. If these

issues are unresolved, the FDA may choose to not allow the clinical trials to commence. There is no guarantee that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Clinical trials are conducted under protocols detailing the objectives of the trials, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND prior to beginning the trial. Each trial must be reviewed and approved by an independent Institutional

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Research Board for each investigative site before it can begin at that site. Subjects must provide informed consent for all trials.

In Phase 1, the initial introduction of the drug into human subjects, the drug is usually tested for safety or adverse effects, dosage tolerance, pharmacokinetics, and pharmacologic action;

Phase 2 usually involves controlled trials in a limited patient population to:

evaluate preliminarily the efficacy of the drug for a specific, targeted condition,

determine dosage tolerance and appropriate dosage for further trials, and

identify possible adverse effects and safety risks.

Phase 3 trials generally further evaluate clinical efficacy and test further for safety within an expanded patient population with considerations of statistical design and power.

Phase 1, 2, and 3 testing may not be completed successfully within any specified period, or at all. We, an Institutional Review Board, or the FDA, may suspend or terminate clinical trials at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk. Additional nonclinical toxicology studies are required after clinical trials have begun. Our clinical testing program may be delayed or terminated due to factors such as:

unforeseen safety issues in the clinical trials and/or the continuing nonclinical toxicology studies;

inability to recruit patients at the rate we expect;

failure by the subjects and/or the investigators to adhere to protocol requirements;

inability to collect the information required to assess patients adequately for safety and efficacy; and

insufficient evidence of efficacy.

The results of the nonclinical and clinical studies, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA as part of an NDA or BLA for review and potential approval prior to the marketing and commercial shipment of the product. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure, and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product s continued safety, purity, and potency. In most cases, the NDA or BLA must be accompanied by a substantial user fee. The FDA also will inspect the manufacturing facility used to produce the product for compliance with cGMP regulations. The FDA may deny an NDA or BLA if all applicable regulatory criteria are not satisfied or may require additional clinical, toxicology or manufacturing data. Even after an NDA or BLA results in approval to market a product, the FDA may limit the indications or place other limitations that restrict the commercial application of the product. The FDA may issue a not approvable response to any NDA or BLA we or our collaborators may submit for a variety of reasons, including insufficient evidence of safety and/or efficacy or inadequate manufacturing procedures.

After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. The FDA may require

additional clinical testing, or Phase 4 clinical trials, to be conducted after initial marketing approval. The FDA may withdraw product approval if compliance with regulatory standards and/or conditions of the marketing approval is not maintained or if safety problems occur after the product reaches the market. In addition, the FDA requires surveillance programs to monitor the consistency of manufacturing and the safety of approved products that have been commercialized. Holders of an approved NDA are required to report certain adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling. The agency has the power to require changes in labeling or to prevent further marketing of a product based on new data that may arise after commercialization. Also, new federal, state, or local government requirements may be established that could delay or prevent regulatory approval of our products under development.

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It may take many years and the expenditure of substantial resources to evaluate fully the safety and efficacy of a drug candidate in nonclinical and clinical studies, to qualify appropriate drug product formulations, and to ensure manufacturing processes are compliant with regulations. Data obtained in nonclinical studies or early clinical studies may not be indicative of results that might be obtained in later clinical trials that are often critical to the regulatory approval process. Formulation and/or manufacturing changes may cause delays in the development plan or require re-testing. Many of the activities may be subject to varying interpretations that could limit, delay, or prevent regulatory approval.

We will also be subject to a variety of foreign regulations governing clinical trials and the marketing and sale of our products. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. For marketing outside the U.S., we are also subject to foreign regulatory requirements governing human clinical trials. The requirements governing the conduct of clinical trials, product licensing, approval, pricing, and reimbursement vary greatly from country to country.

In addition to regulations enforced by the FDA, we are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other present and potential future federal, state, or local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state, federal, and local regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources.

Our collaborators under the various license agreements we have completed have assumed responsibility for regulatory issues pertinent to any drug candidates or marketed products that may arise from our collaborations.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of any of our drug candidates. We currently rely and expect to continue to rely on third parties for the manufacture of our drug candidates for preclinical and clinical development. We currently source our bulk drug manufacturing requirements from one contract manufacturer through the issuance of purchase orders on an as-needed basis. We depend and will continue to depend on our contract manufacturers to manufacture our drug candidates in accordance with cGMP regulations for use in clinical trials. We will ultimately depend on contract manufacturers for the manufacture of our products for commercial sale. Contract manufacturers are subject to extensive governmental regulation.

Under our collaborative agreements with Merck KGaA, Merck & Co., and Novartis, our collaborators are responsible for manufacturing the drug candidates. We believe each collaborator purchases bulk drugs from a contract manufacturer.

Competition

We are developing our TLR-targeted drug candidates for use in the treatment of infectious diseases, autoimmune diseases, cancer and asthma and allergies, and as vaccine adjuvants. For all of the disease areas in which we are developing potential therapies, we face competition from other companies developing products involving TLR targeted compounds as well as non-TLR targeted therapies. Some of these non-TLR targeted therapies have been in

development or commercialized for years, in some cases by large, well established pharmaceutical companies. Many of the marketed therapies have been accepted by the medical community, patients, and third-party payors. Our ability to compete may be affected by the previous adoption of such therapies by the medical community, patients, and third party payors. Additionally, in some instances, insurers and other third-party payors seek to encourage the use of generic products, which makes branded products, such as our drug candidates, potentially less attractive, from a cost perspective, to buyers.

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With respect to the development of products involving stimulation of the immune system, there are a number of companies, both privately and publicly held, that are actively engaged in the discovery, development, and commercialization of products and technologies involving TLR-targeted compounds that compete with our technologies and drug candidates, including compounds targeting TLRs 7, 8 or 9. Our principal competitors developing TLR-targeted compounds include: Pfizer, Inc., which acquired Coley Pharmaceutical Group in November 2007; Dynavax Technologies Corporation; and Anadys Pharmaceutical, Inc. We are also aware that the following companies are developing TLR-targeted compounds: Cytos Biotechnology AG; Eisai, Inc.; GlaxoSmithKline plc; Hemispherx Biopharma, Inc.; Innate Pharma SA; Intercell AG; Opsona Therapeutics Ltd.; and VaxInnate, Inc.

In infectious diseases, Dynavax Technologies Corporation has a preclinical TLR9 agonist lead molecule for hepatitis C treatment.

In autoimmune diseases, Pfizer, Inc., has an on-going Phase 1 clinical trial in healthy volunteers with a TLR antagonist, CPG 52364, for the treatment of lupus, and Dynavax Technologies Corporation has a discovery-stage autoimmune program.

In cancer, Pfizer, Inc., has multiple clinical trials on-going with its TLR9 agonist PF-3512676. In June 2007, Coley Pharmaceutical Group, which has since been acquired by Pfizer, Inc., discontinued certain clinical trials for PF-3512676 in combination with selected cytotoxic agents in lung cancer. Dynavax Technologies Corporation has an ongoing Phase 2 clinical trial in Non-Hodgkin s lymphoma for its TLR9 agonist 1018 ISS as well as a Phase 1 clinical trial in colorectal cancer. In addition, Anadys Pharmaceutical, Inc., has announced that is has initiated a Phase 1 clinical trial in solid tumors for its TLR7 agonist ANA773.

In asthma and allergies, Dynavax Technologies Corporation by itself and in collaboration with AstraZeneca Pharmaceuticals plc, and Pfizer, Inc., in collaboration with sanofi-aventis Groupe have ongoing clinical trials with TLR9 agonists.

Merck & Co. s vaccines using our TLR7, 8 or 9 agonists as adjuvants may compete with vaccines being developed or marketed by GlaxoSmithKline plc, Novartis, Dynavax Technologies Corporation, VaxInnate, Inc., Intercell AG, and Cytos Biotechnology AG.

We recognize that other companies, including large pharmaceutical companies, may be developing or have plans to develop competitive products and technology. Many of our competitors have substantially greater financial, technical, and human resources than we have. In addition, many of our competitors have significantly greater experience than we have in undertaking preclinical studies and human clinical trials of new pharmaceutical products, obtaining FDA and other regulatory approvals of products for use in health care and manufacturing, marketing and selling approved products.

Competition among these products and therapies will be based, among other things, on product efficacy, safety, reliability, availability, price, and patent position.

The timing of market introduction of our products and competitive products will also affect competition among products. We also expect the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market to be an important competitive factor. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes and to secure sufficient capital resources for the often substantial period between technological conception and commercial sales.

Employees

As of February 29, 2008, we employed 38 individuals full-time. Of our 38 employees, 25 are engaged in research and development and 21 hold a Ph.D., M.D., or equivalent degree. None of our employees are covered by a collective bargaining agreement, and we consider relations with our employees to be good.

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Information Available on the Internet

Our internet address is www.iderapharma.com. The contents of our website are not part of this Annual Report on Form 10-K and our internet address is included in this document as an inactive textual reference. We make available free of charge through our web site our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 12(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission.

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

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this annual report on Form 10-K before purchasing our common stock. If any of the following risks actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock.

Risks Relating to Our Financial Results and Need for Financing

We have incurred substantial losses and expect to continue to incur losses. We will not be successful unless we reverse this trend.

We have incurred losses in every year since our inception, except for 2002 when our recognition of revenues under a license and collaboration agreement resulted in our reporting net income for that year. As of December 31, 2007, we had an accumulated deficit of $342.7 million. We have incurred losses of $82.5 million since January 1, 2001. We also incurred losses of $260.2 million prior to December 31, 2000 during which time we were primarily involved in the development of antisense technology. These losses, among other things, have had and will continue to have an adverse effect on our stockholders equity, total assets and working capital.

We have never had any products of our own available for commercial sale and have received no revenues from the sale of drugs. To date, almost all of our revenues have been from collaborative and license agreements. We have devoted substantially all of our efforts to research and development, including clinical trials, and we have not completed development of any drugs. Because of the numerous risks and uncertainties associated with developing drugs, we are unable to predict the extent of any future losses, whether or when any of our products will become commercially available, or when we will become profitable, if at all. We may incur substantial operating losses in future periods.

We will need additional financing, which may be difficult to obtain. Our failure to obtain necessary financing or doing so on unattractive terms could adversely affect our research and development programs and other operations.

We will require substantial funds to conduct research and development, including preclinical testing and clinical trials of our drug candidates. We will also require substantial funds to conduct regulatory activities and to establish commercial manufacturing, marketing and sales capabilities. We believe that, based on our current operating plan, our existing cash, cash equivalents and short-term investments, including the $39.7 million upfront payment that we received in February 2008 under our agreement with Merck KGaA, will be sufficient to fund our operations at least through December 31, 2009.

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We will need to raise additional funds to operate our business beyond such time, including completing any on-going clinical trials involving IMO-2125 or other drug candidates we may develop. We believe that the key factors that will affect our ability to obtain additional funding are:

- the success of our clinical and preclinical development programs;
- the success of our existing strategic collaborations with Merck KGaA, Merck & Co. and Novartis;
- the cost, timing and outcome of regulatory reviews;
- the receptivity of the capital markets to financings by biotechnology companies; and
- our ability to enter into additional strategic collaborations with biotechnology and pharmaceutical companies and the success of such collaborations.

If we cannot obtain adequate funds, we may terminate, modify or delay preclinical or clinical trials of one or more of our drug candidates, fail to establish or delay the establishment of manufacturing, sale or marketing capabilities, or curtail research and development programs for new drug candidates.

Additional financing may not be available to us when we need it or may not be available to us on favorable terms. We could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, drug candidates or drugs that we would otherwise pursue on our own. In addition, if we raise additional funds by issuing equity securities, our then existing stockholders will experience dilution. The terms of any financing may adversely affect the holdings or the rights of existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, and are likely to include rights that are senior to the holders of our common stock. Any additional debt financing or equity that we raise may contain terms, such as liquidation and other preferences, or liens or other restrictions on our assets, which are not favorable to us or our stockholders. If we are unable to obtain adequate funding on a timely basis or at all, we may be required to significantly curtail one or more of our discovery or development programs. For example, we significantly curtailed expenditures on our research and development programs during 1999 and 2000 because we did not have sufficient funds available to advance these programs at planned levels.

Risks Relating to Our Business, Strategy and Industry

We are depending heavily on the success of our our lead drug candidate for infectious diseases, IMO-2125, and our collaborative programs. If we or our collaborators are unable to successfully develop and commercialize our drug candidates, or experience significant delays in doing so, our business will be materially harmed.

We are investing a significant portion of our time and financial resources in the development of our clinical stage lead drug candidate for infectious diseases, IMO-2125. We anticipate that our ability to generate product revenues will depend heavily on the successful development and commercialization of IMO-2125 and other drug candidates including drug candidates being developed by our collaborators. The commercial success of these drug candidates will depend on several factors, including the following:

- acceptable safety profile during clinical trials;
- demonstration of statistically recognized efficacy in clinical trials;

ability to combine IMO-2125 safely and successfully with other antiviral agents;

receipt of marketing approvals from the FDA and equivalent foreign regulatory authorities;

establishment of commercial manufacturing arrangements with third-party manufacturers;

the successful commercial launch of the drug candidates, whether alone or in collaboration with other products;

acceptance of the products by the medical community and third-party payors;

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competition from other companies and their therapies;

successful protection of our intellectual property rights from competing products in the United States and abroad; and

a continued acceptable safety and efficacy profile of our drug candidates following approval.

Our efforts to commercialize IMO-2125 are at an early stage, as we are currently conducting the initial Phase 1 safety clinical trial of this drug candidate in a defined patient population. If we are not successful in commercializing this or our other drug candidates, or are significantly delayed in doing so, our business will be materially harmed.

If our clinical trials are unsuccessful, or if they are delayed or terminated, we may not be able to develop and commercialize our products.

In order to obtain regulatory approvals for the commercial sale of our products, we are required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. Clinical trials are lengthy, complex and expensive processes with uncertain results. We may not be able to complete any clinical trial of a potential product within any specified time period. Moreover, clinical trials may not show our potential products to be both safe and efficacious. The FDA and other regulatory authorities may not approve any of our potential products for any indication. We may not be able to obtain authority from the FDA or other equivalent foreign regulatory agencies to complete these trials or commence and complete any other clinical trials.

The results from preclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced stage clinical trials. Furthermore, interim results of a clinical trial do not necessarily predict final results and failure of any of our clinical trials can occur at any stage of testing. Companies in the biotechnology and pharmaceutical industries, including companies with greater experience in preclinical testing and clinical trials than we have, have suffered significant setbacks in clinical trials, even after demonstrating promising results in earlier trials. For example in June 2007, Coley Pharmaceutical Group, which since has been acquired by Pfizer, Inc., discontinued four clinical trials in lung cancer for PF-3512676, its investigational TLR9 agonist compound, in combination with cytotoxic chemotherapy. In addition, in January 2007, Coley Pharmaceutical Group announced that it had suspended its development of a TLR9 agonist, Actilon®, for hepatitis C virus infection. In July 2007, Anadys Pharmaceuticals, Inc. and its partner Novartis announced that they had decided to discontinue the development of ANA975, the investigational TLR7 agonist compound for hepatitis C virus infection.

There are to date few data on the long-term clinical safety of our lead compounds under conditions of prolonged use in humans, or on any long-term consequences subsequent to human use. Effects seen in preclinical studies, even if not observed in clinical trials, may result in limitations or restrictions on our clinical trials. We may experience numerous unforeseen events during, or as a result of, preclinical testing, nonclinical testing, or the clinical trial process that could delay or inhibit our ability to receive regulatory approval or to commercialize our products, including:

regulators or Institutional Review Boards may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;

nonclinical or clinical data may not be readily interpreted, which may lead to delays and/or misinterpretation;

our nonclinical tests, including toxicology studies, or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical testing or clinical trials or we may abandon projects that we expect may not be promising;

the rate of enrollment or retention of patients in our clinical trials may be less than expected;

we might have to suspend or terminate our clinical trials if the participating patients experience serious adverse events or undesirable side effects or are exposed to unacceptable health risks;

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regulators or Institutional Review Boards may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, including any issues identified through inspections of manufacturing or clinical trial operations or clinical trial sites;

regulators may hold or suspend our clinical trials while collecting supplemental information on, or clarification of, our clinical trials or other clinical trials, including trials conducted in other countries or trials conducted by other companies;

we, along with our collaborators and subcontractors, may not employ, in any capacity, persons who have been debarred under the FDA s Application Integrity Policy. Employment of such debarred persons, even if inadvertently, may result in delays in the FDA s review or approval of our products, or the rejection of data developed with the involvement of such person(s);

the cost of our clinical trials may be greater than we currently anticipate; and

our products may not cause the desired effects or may cause undesirable side effects or our products may have other unexpected characteristics.

As an example, in 1997, after reviewing the results from the clinical trial of GEM91, a first generation antisense compound and our lead drug candidate at the time, we determined not to continue the development of GEM91 and suspended clinical trials of this drug candidate.

The rate of completion of clinical trials is dependent in part upon the rate of enrollment of patients. For example, in Stage A of our Phase 2 trial of IMO-2055 in renal cell cancer, enrollment was slower than projected due to the recent approval of two new therapies, Sutent® and Nexavar®, developed by other companies for treatment of the same patient populations. Patient accrual is a function of many factors, including:

the size of the patient population;

the proximity of patients to clinical sites;

the eligibility criteria for the study;

the nature of the study;

the existence of competitive clinical trials; and

the availability of alternative treatments.

We do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, if at all. Significant clinical trial delays also could allow our competitors to bring products to market before we do and impair our ability to commercialize our products.

Delays in commencing clinical trials of potential products could increase our costs, delay any potential revenues and reduce the probability that a potential product will receive regulatory approval.

Our drug candidates and our collaborators drug candidates will require preclinical and other nonclinical testing and extensive clinical trials prior to submission of any regulatory application for commercial sales. In 2007, we

commenced a new Phase 1b clinical trial of IMO-2055 in oncology, and we commenced a Phase 1 clinical trial of IMO-2125 for chronic hepatitis C virus infection. In conducting clinical trials, we cannot be certain that any planned clinical trial will begin on time, if at all. Delays in commencing clinical trials of potential products could increase our product development costs, delay any potential revenues and reduce the probability that a potential product will receive regulatory approval.

Commencing clinical trials may be delayed for a number of reasons, including delays in:

manufacturing sufficient quantities of drug candidate that satisfy the required quality standards for use in clinical trials;

demonstrating sufficient safety to obtain regulatory approval for conducting a clinical trial;

reaching an agreement with any collaborators on all aspects of the clinical trial;

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reaching agreement with contract research organizations, if any, and clinical trial sites on all aspects of the clinical trial;

resolving any objections from the FDA or any regulatory authority on an IND application or proposed clinical trial design;

obtaining Institutional Review Board approval for conducting a clinical trial at a prospective site; and

enrolling patients in order to commence the clinical trial.

The technologies on which we rely are unproven and may not result in any approved and marketable products.

Our technologies or therapeutic approaches are relatively new and unproven. We have focused our efforts on the research and development of RNA- and DNA-based compounds targeted to TLRs. Neither we nor any other company have obtained regulatory approval to market such compounds as therapeutic drugs, and no such products currently are being marketed. It is unknown whether the results of preclinical studies with TLR-targeted compounds will be indicative of results that may be obtained in clinical trials, and results we have obtained in the initial small-scale clinical trials we have conducted to date may not be predictive of results in subsequent large-scale trials. Further, the chemical and pharmacological properties of RNA- and DNA-based compounds targeted to TLRs may not be fully recognized in preclinical and small-scale clinical trials, and such compounds may interact with human biological systems in unforeseen, ineffective, or harmful ways that we have not yet identified. As a result of these factors, we may never succeed in obtaining a regulatory approval to market any product. Furthermore, the commercial success of any of our products for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third party payors as clinically useful, safe, and cost-effective. In addition, if products based upon TLR technology being developed by our competitors have negative clinical trial results or otherwise are viewed negatively, the perception of our TLR technology and market acceptance of our products could be impacted negatively. For example, we are pursuing an indication for treatment of chronic hepatitis C virus infection for IMO-2125 and commenced a Phase 1 clinical trial of IMO-2125 in patients with chronic hepatitis C virus infection in the third quarter of 2007. Pfizer, Inc. and Anadys Pharmaceuticals, Inc. each have performed early clinical trials of TLR-targeted compounds for the treatment of chronic hepatitis C virus infection, and both programs have been discontinued. We cannot be certain whether such discontinuations will negatively impact the perception of our TLR technology.

Our efforts to educate the medical community on our potentially unique approaches may require greater resources than would be typically required for products based on conventional technologies or therapeutic approaches. The safety, efficacy, convenience and cost-effectiveness of our products as compared to competitive products will also affect market acceptance.

We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than us.

The biotechnology industry is highly competitive and characterized by rapid and significant technological change. We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies. Some of these organizations are pursuing products based on technologies similar to our technologies. Other of these organizations have developed and are marketing products, or are pursuing other technological approaches designed to produce products, that are competitive with our drug candidates in the therapeutic effect these competitive products have on diseases targeted by our drug candidates. Our competitors may discover, develop or commercialize products or other novel technologies that are more effective,

safer or less costly than any that we are developing. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. As examples, the FDA recently approved drugs developed by other companies, Sutent® and Nexavar®, for use in renal cell cancer, which is the indication for which we are evaluating IMO-2055 monotherapy in our Phase 2 trial. Pfizer, Inc., is conducting clinical trials of PF-3512676, a TLR9 agonist for treating cancer. In addition, Dynavax Technologies Corporation has announced initiation of a clinical trial for its TLR9 agonist 1018 ISS for cancer. Both Pfizer, Inc., and Dynavax Technologies Corporation have clinical programs, either independently or with

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collaborators, in therapeutic fields other than cancer, such as asthma and allergy treatments and for use as vaccine adjuvants, that also potentially compete with our drug candidates.

Many of our competitors are substantially larger than we are and have greater capital resources, research and development staffs and facilities than we have. In addition, many of our competitors are more experienced than we are in drug discovery, development and commercialization, obtaining regulatory approvals and drug manufacturing and marketing.

We anticipate that the competition with our products and technologies will be based on a number of factors including product efficacy, safety, availability and price. The timing of market introduction of our products and competitive products will also affect competition among products. We expect the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market to be important competitive factors. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes and protect our intellectual property, and to secure sufficient capital resources for the period between technological conception and commercial sales.

Competition for technical and management personnel is intense in our industry, and we may not be able to sustain our operations or grow if we are unable to attract and retain key personnel.

Our success is highly dependent on the retention of principal members of our technical and management staff, including Dr. Sudhir Agrawal. Dr. Agrawal serves as our Chief Executive Officer and Chief Scientific Officer. Dr. Agrawal has made significant contributions to the field of oligonucleotide-based drug candidates, and has led the discovery and development of our compounds targeted to TLRs. He is named as an inventor on over 380 patents and patent applications worldwide. Dr. Agrawal provides us leadership for management, research and development activities. The loss of Dr. Agrawal s services would be detrimental to our ongoing scientific progress and the execution of our business plan.

We are a party to an employment agreement with Dr. Agrawal that expires on October 19, 2010, but automatically extends annually for an additional year. This agreement may be terminated by us or Dr. Agrawal for any reason or no reason at any time upon notice to the other party. We do not carry key man life insurance for Dr. Agrawal.

Furthermore, our future growth will require hiring a number of qualified technical and management personnel. Accordingly, recruiting and retaining such personnel in the future will be critical to our success. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. If we are not able to continue to attract and retain, on acceptable terms, the qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or growth.

Regulatory Risks

We may not be able to obtain marketing approval for products resulting from our development efforts.

All of the drug candidates that we are developing or may develop in the future will require additional research and development, extensive preclinical studies and clinical trials, and regulatory approval prior to any commercial sales. This process is lengthy, often taking a number of years, is uncertain, and is expensive. Since our inception, we have conducted clinical trials of a number of compounds. Currently, we are conducting clinical trials of IMO-2125 and IMO-2055.

We may need to address a number of technological challenges in order to complete development of our products. Moreover, these products may not be effective in treating any disease or may prove to have undesirable or unintended side effects, unintended alteration of the immune system over time, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

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We are subject to comprehensive regulatory requirements, which are costly and time consuming to comply with; if we fail to comply with these requirements, we could be subject to adverse consequences and penalties.

The testing, manufacturing, labeling, advertising, promotion, export and marketing of our products are subject to extensive regulation by governmental authorities in Europe, the United States and elsewhere throughout the world.

In general, submission of materials requesting permission to conduct clinical trials may not result in authorization by the FDA or any equivalent foreign regulatory agency to commence clinical trials. Further, permission to continue ongoing trials may be withdrawn by the FDA or other regulatory agencies at any time after initiation, based on new information available after the initial authorization to commence clinical trials. In addition, submission of an application for marketing approval to the relevant regulatory agency following completion of clinical trials may not result in the regulatory agency approving the application if applicable regulatory criteria are not satisfied, and may result in the regulatory agency requiring additional testing or information.

Any regulatory approval of a product may contain limitations on the indicated uses for which the product may be marketed or requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Any product for which we obtain marketing approval, along with the facilities at which the product is manufactured, any post-approval clinical data and any advertising and promotional activities for the product will be subject to continual review and periodic inspections by the FDA and other regulatory agencies.

Both before and after approval is obtained, violations of regulatory requirements may result in:

- the regulatory agency s delay in approving, or refusal to approve, an application for marketing of a product;
- restrictions on our products or the manufacturing of our products;
- withdrawal of our products from the market;
- warning letters;
- voluntary or mandatory recall;
- fines;
- suspension or withdrawal of regulatory approvals;
- product seizure;
- refusal to permit the import or export of our products;
- injunctions or the imposition of civil penalties; and
- criminal penalties.

We have only limited experience in regulatory affairs and our products are based on new technologies; these factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have only limited experience in filing the applications necessary to gain regulatory approvals. Moreover, the products that result from our research and development programs will likely be based on new technologies and new

therapeutic approaches that have not been extensively tested in humans. The regulatory requirements governing these types of products may be more rigorous than for conventional drugs. As a result, we may experience a longer regulatory process in connection with obtaining regulatory approvals of any product that we develop.

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Risks Relating to Collaborators

We need to establish additional collaborative relationships in order to succeed.

If we do not reach agreements with additional collaborators in the future, we may fail to meet our business objectives. We believe collaborations can provide us with expertise and resources. If we cannot enter into additional collaboration agreements, we may not be able to obtain the expertise and resources necessary to achieve our business objectives. We face, and will continue to face, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements. The terms of any collaborations or other arrangements that we establish, if any, may not be favorable to us.

The failure of these collaborative relationships could delay our drug development or impair commercialization of our products and could materially harm our business and might accelerate our need for additional capital.

Any collaboration that we enter into may not be successful. The success of our collaboration arrangements, if any, will depend heavily on the efforts and activities of our collaborators. Possible future collaborations have risks, including the following:

- disputes may arise in the future with respect to the ownership of rights to technology developed with future collaborators;
- disagreements with future collaborators could delay or terminate the research, development or commercialization of products, or result in litigation or arbitration;
- future collaboration agreements are likely to be for fixed terms and subject to termination by our collaborators in the event of a material breach or lack of scientific progress by us;
- future collaborators are likely to have the first right to maintain or defend our intellectual property rights and, although we would likely have the right to assume the maintenance and defense of our intellectual property rights if our collaborators do not, our ability to do so may be compromised by our collaborators acts or omissions;
- future collaborators may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability;
- future collaborators may change the focus of their development and commercialization efforts. Pharmaceutical and biotechnology companies historically have re-evaluated their priorities following mergers and consolidations, which have been common in recent years in these industries. The ability of our products to reach their potential could be limited if future collaborators decrease or fail to increase spending relating to such products;
- future collaborators may underfund or not commit sufficient resources to the testing, marketing, distribution or development of our products; and
- future collaborators may develop alternative products either on their own or in collaboration with others, or encounter conflicts of interest or changes in business strategy or other business issues, which could adversely affect their willingness or ability to fulfill their obligations to us.

Given these risks, it is possible that any collaborative arrangements into which we enter may not be successful.

Our existing collaborations and any collaborations we enter into in the future may not be successful.

An important element of our business strategy includes entering into strategic collaborations with corporate collaborators, primarily large pharmaceutical companies, for the development, commercialization, marketing and distribution of some of our drug candidates. 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 treatment of cancer, excluding cancer vaccines. In December 2006, we entered into an exclusive license and research collaboration with Merck & Co. to research, develop, and commercialize vaccine products containing our

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TLR7, 8, and 9 agonists in the fields of cancer, infectious diseases, and Alzheimer s disease. In May 2005, we entered into a collaboration with Novartis to discover, develop and potentially commercialize TLR9 agonists that are identified as potential treatments for asthma and allergies. The failure of these collaborations or any others we enter into in the future could delay our drug development or impair commercialization of our products and could materially harm our business and might accelerate our need for additional capital.

The success of our collaboration arrangements, if any, will depend heavily on the efforts and activities of our collaborators. Our existing collaborations have risks, including the following:

- our collaborators control the development of the drug candidates being developed with our technologies and compounds including the timing of development;
- our collaborators may control the public release of information regarding the developments, and we may not be able to make announcements or data presentations on a schedule favorable to us;
- disputes may arise in the future with respect to the ownership of rights to technology developed with our collaborators;
- disagreements with our collaborators could delay or terminate the research, development or commercialization of products, or result in litigation or arbitration;
- we may have difficulty enforcing the contracts if any of our collaborators fail to perform;
- our collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect the perception of us in the business or financial communities;
- our collaboration agreements are likely to be for fixed terms and subject to termination by our collaborators in the event of a material breach or lack of scientific progress by us;
- our collaborators may have the first right to maintain or defend our intellectual property rights and, although we would likely have the right to assume the maintenance and defense of our intellectual property rights if our collaborators do not, our ability to do so may be compromised by our collaborators acts or omissions;
- our collaborators may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability;
- our collaborators may change the focus of their development and commercialization efforts. Pharmaceutical and biotechnology companies historically have re-evaluated their priorities following mergers and consolidations, which have been common in recent years in these industries. The ability of our products to reach their potential could be limited if our collaborators decrease or fail to increase spending relating to such products;
- our collaborators may underfund or not commit sufficient resources to the testing, marketing, distribution or development of our products; and
- our collaborators may develop alternative products either on their own or in collaboration with others, or encounter conflicts of interest or changes in business strategy or other business issues, which could adversely affect their willingness or ability to fulfill their obligations to us.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Such terminations or expirations may adversely affect us financially and could harm our business reputation in the event we elect to pursue collaborations that ultimately expire or are terminated in such a manner.

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Risks Relating to Intellectual Property

If we are unable to obtain patent protection for our discoveries, the value of our technology and products will be adversely affected.

Our patent positions, and those of other drug discovery companies, are generally uncertain and involve complex legal, scientific and factual questions. Our ability to develop and commercialize drugs depends in significant part on our ability to:

obtain patents;

obtain licenses to the proprietary rights of others on commercially reasonable terms;

operate without infringing upon the proprietary rights of others;

prevent others from infringing on our proprietary rights; and

protect trade secrets.

We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may be issued in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thus reducing any advantage provided by the patent.

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, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications.

Third parties may own or control patents or patent applications and require us to seek licenses, which could increase our development and commercialization costs, or prevent us from developing or marketing products.

We may not have rights under some patents or patent applications related to our products. Third parties may own or control these patents and patent applications in the United States and abroad. Therefore, in some cases, to develop, manufacture, sell or import some of our products, we or our collaborators may choose to seek, or be required to seek, licenses under third party patents issued in the United States and abroad or under patents that might issue from United States and foreign patent applications. In such an event, we would be required to pay license fees or royalties or both to the licensor. If licenses are not available to us on acceptable terms, we or our collaborators may not be able to develop, manufacture, sell or import these products.

We may lose our rights to patents, patent applications or technologies of third parties if our licenses from these third parties are terminated. In such an event, we might not be able to develop or commercialize products covered by the licenses.

Currently, we have not in-licensed any patents or patent applications related to our TLR-targeted drug candidate programs. However in the field of antisense technology we are party to five royalty-bearing license agreements under which we have acquired rights to patents, patent applications and technology of third parties. Under these licenses we are obligated to pay royalties on net sales by us of products or processes covered by a valid claim of a patent or patent application licensed to us. We also are required in some cases