IDERA PHARMACEUTICALS, INC.
Form 10-K
March 11, 2009

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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, 2008
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 **(State or other jurisdiction of incorporation or organization)**	**04-3072298** **(I.R.S. Employer Identification No.)**
167 Sidney Street **Cambridge, Massachusetts** **(Address of principal executive offices)**	**02139** **(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 $321,536,000 based on the last sale price of the registrant s common stock as reported on the NASDAQ Global Market on June 30, 2008. As of February 26, 2009, the registrant had 23,422,525 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 16, 2009 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 and inflammatory 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 drug candidates in multiple disease areas simultaneously. We are advancing some of these applications through internal programs, and we seek to advance other applications through collaborative alliances with pharmaceutical companies. Collaborators provide the necessary resources and drug development experience to advance our compounds in their programs. Upfront payments and milestone payments received from collaborations help to provide us with the financial resources for our internal research and development programs.

Our internal programs are focused on developing TLR-targeted drug candidates for the potential treatment of infectious diseases, autoimmune and inflammatory diseases, and cancer. IMO-2125, a TLR9 agonist, is our lead drug candidate for infectious diseases. We are conducting a Phase 1 clinical trial of IMO-2125 in patients with chronic hepatitis C virus, or HCV, 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 HCV RNA levels and on parameters of immune system activation. We also plan to conduct a clinical trial of IMO-2125 to assess the safety of IMO-2125 in combination with ribavirin in treatment-naïve patients with chronic HCV infection. This clinical trial also will evaluate the effects of IMO-2125 and ribavirin combination treatment on HCV RNA levels and on 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/or TLR8. We refer to our TLR7 and TLR8 agonists as **s**tabilized **i**mmune **m**odulatory **RNA** , or SIMRA, compounds. We are evaluating the mechanism of action of our SIMRA compounds in preclinical studies in human cell-based assays and *in vivo* in non-human primates.

In our autoimmune and inflammatory disease program, we have identified DNA-based compounds that act as antagonists of TLR7 and TLR9. We have evaluated these compounds in mouse models of lupus, rheumatoid arthritis, multiple sclerosis, psoriasis, colitis, and pulmonary inflammation. We have selected IMO-3100 as a lead TLR antagonist drug candidate, and are currently conducting preclinical development studies in anticipation of submitting an Investigational New Drug, or IND, application to the United States Food and Drug Administration, or FDA, by the end of 2009. We have formed an Autoimmune Disease Scientific Advisory Board to assist us in the clinical development strategy for IMO-3100 and other antagonist candidates in autoimmune and inflammatory diseases.

Our cancer treatment research program is focused on potential applications of our TLR7 and/or TLR8 agonists. We are studying our TLR7 and TLR8 agonists in preclinical models of cancer and have observed antitumor activity as

monotherapy and in combination with selected targeted agents.

We are also collaborating with three pharmaceutical companies to advance our TLR-targeted compounds in additional 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

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cancer vaccines. Under the agreement, we exclusively licensed our clinical stage drug candidates IMO-2055, a TLR9 agonist, and IMO-2125, as well as other TLR9 agonists, for the treatment of cancer, excluding cancer vaccines. We continue to support Merck KGaA in its clinical development plan. At present, we are conducting on behalf of Merck KGaA a clinical trial of IMO-2055 in combination with Erbitux® and Camptosar® in patients with colorectal cancer, and a clinical trial of IMO-2055 in combination with Avastin® and Tarceva® in patients with non-small cell lung cancer. In February 2009, we achieved a milestone under our agreement with Merck KGaA upon the dosing of the first patient in the Erbitux/Camptosar clinical trial. Under the terms of the agreement, we are entitled to receive a payment of 3.0 million (approximately $3.8 million) from Merck KGaA in 2009.

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 research collaboration to generate novel agonists targeting TLR7 and TLR8, which may incorporate both Merck & Co. and Idera chemistry, for use in Merck & Co. s vaccines for cancer, infectious diseases and Alzheimer s disease. In May 2008, we achieved a preclinical milestone under our collaboration with Merck & Co. involving one of our novel TLR9 agonists used as an adjuvant in cancer vaccines. In November 2008, Merck & Co. extended the research collaboration, which was originally for two years, for an additional year to December 2009.

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 September 2008, we achieved a milestone under our Novartis collaboration, related to the initiation of a Phase 1 clinical trial by Novartis of QAX935, a novel agonist of TLR9.

Our Business Strategy

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

We have entered into collaborative alliances for application of our technology in multiple therapeutic areas. We believe that 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 up-front payments and milestone payments that have helped to finance our internal 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 HCV infection, our development of IMO-3100 continues in anticipation of an IND submission, and our preclinical programs move forward in infectious diseases, autoimmune and inflammatory 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 compounds, to populate our expanding research and development programs and to support our collaborations.

Overview of the Human Immune System

The immune system protects the body by working through various mechanisms to recognize and eliminate bacteria, viruses and other infectious agents, referred to as pathogens, and abnormal cells, such as cancer cells. These mechanisms initiate a series of signals resulting in stimulation of the immune system in response to the

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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 infection. The adaptive immune system does this through the recognition by certain immune cells of specific proteins, called antigens, which are part of the pathogen or abnormal cell. This process is initiated through signals produced by the innate immune system. Upon recognition of a foreign antigen, which could come from pathogens or from cancer cells, the adaptive immune system produces antibodies and antigen-specific immune cells that specifically detect and destroy cells that contain the antigen. This response is referred to as an antigen-specific immune response. An antigen-specific immune response normally takes several weeks to develop the first time. However, once developed, the adaptive immune system remembers the antigen. In this manner, if the pathogen again infects the body, the presence of the memory immunity will allow the adaptive immune system to respond again, this time in a matter of days.

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 based on drug candidates that are agonists of TLR9. These candidates 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 TLR9 agonists can be changed by modifying the structure. Our ability to change immunological activity by modifying the chemical structure allows us to create a growing portfolio of TLR9 agonist drug candidates that are potentially useful for treating or preventing different diseases.

TLR7 and TLR8 Agonists

We are designing and creating novel synthetic RNA-based compounds that are agonists of TLR7 and/or TLR8. These RNA-based compounds are designed to mimic viral RNA. In preclinical studies in cell culture and animal models, these TLR7 and/or TLR8 agonists induced immune responses that we believe may be applicable to the treatment of cancer and infectious diseases and as vaccine adjuvants. We are studying our TLR7 and TLR8 agonists

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in preclinical models of cancer and have observed antitumor activity as monotherapy and in combination with selected targeted agents.

TLR7 and TLR9 Antagonists

We are creating novel classes of drug candidates that are designed to be antagonists of TLR7 and TLR9. Recent preclinical studies from independent researchers have suggested TLR7 and TLR9 may play a role in certain autoimmune and inflammatory 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 drug candidates in preclinical mouse models of human autoimmune and inflammatory diseases including lupus, rheumatoid arthritis, multiple sclerosis, psoriasis, colitis, and pulmonary inflammation. In these models, treatment with our antagonist drug candidates was associated with improvement in a number of disease parameters.

Research and Development Programs

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

INTERNAL 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 and Inflammatory Diseases		
Lupus, Rheumatoid Arthritis, Multiple Sclerosis, Psoriasis, Colitis	IMO-3100 (dual TLR7/TLR9 antagonist)	Preclinical Development
Oncology		
Solid Tumor Cancers	TLR7, TLR8 agonists	Research

COLLABORATIVE ALLIANCES

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
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®	Phase 1b Clinical Trial
Vaccine Adjuvants: TLR7, 8, 9 agonists in collaboration with Merck & Co.		

Cancer	TLR7, 8 and 9 agonists	Research
Infectious Disease	TLR7, 8 and 9 agonists	Research
Alzheimer s Disease	TLR7, 8 and 9 agonists	Research
Respiratory Diseases: TLR9 agonists in collaboration with Novartis		
Asthma, Allergies	QAX935 (IMO-2134)	Phase 1 Clinical Trial

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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 HCV infection.

Hepatitis C IMO-2125. Currently, the standard of care treatment for chronic HCV infection is based on therapies that include a single recombinant interferon protein. We and others have shown in preclinical studies that 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 advantages over recombinant interferon for the treatment of chronic HCV 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 non-human primates dosed with IMO-2125 showed potent activity for inhibiting HCV RNA production in cell-based assays.

In May 2007, we submitted an IND for IMO-2125 to the FDA, and in September 2007, we initiated a Phase 1 clinical trial of IMO-2125 in patients with chronic HCV infection who have not responded to the current standard of care therapy. We are currently recruiting patients 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. In addition, the trial is designed to evaluate the effects of IMO-2125 on HCV RNA levels and on parameters of immune system activation.

In this trial, we are enrolling the first five patients per cohort sequentially and allowing each patient to complete at least two weekly injections prior to enrollment of the next patient. Following a safety review of these first five patients in each cohort, the remaining patients of the cohort are enrolled. Due to this enrollment procedure, completion of each cohort has taken longer than anticipated. Currently, we are recruiting patients into the third cohort of the trial. We currently expect interim results from this trial will be available late in 2009.

In addition to the on-going Phase 1 clinical trial of IMO-2125 in HCV patients who have not responded to standard of care therapy, we plan to conduct a clinical trial to assess the safety of IMO-2125 in combination with ribavirin in treatment-naïve patients with chronic HCV infection. This clinical trial also will be designed to evaluate the effects of IMO-2125 and ribavirin combination treatment on HCV RNA levels and on parameters of immune system activation.

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

Viral Diseases. 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/or TLR8. We have discovered structural approaches that stabilize these compounds, which we call SIMRA compounds. We have presented immunological activity profiles from preclinical studies in human cell-based assays and *in vivo* in non-human primates in which our TLR7 and/or TLR8 agonist compounds induced immune responses that might be applicable to the treatment of viral infectious diseases.

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Autoimmune and Inflammatory 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. Independent 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 and inflammatory 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, in a mouse model of rheumatoid arthritis, in a mouse model of multiple sclerosis, in mouse models of psoriasis, in a mouse model of colitis, and in a mouse model of pulmonary inflammation. Data from each of these evaluations showed improvement in a number of disease parameters.

In June 2008, we formed an Autoimmune Disease Scientific Advisory Board with leading researchers in the field of autoimmune diseases to assist us with determining a clinical development strategy for our antagonist candidates. In August 2008, we selected IMO-3100 as a lead antagonist drug candidate and initiated preclinical development studies in anticipation of submitting an IND by the end of 2009.

Oncology

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/or 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 are studying our TLR7 and TLR8 agonists in preclinical models of cancer and have observed antitumor activity as monotherapy and in combination with selected targeted agents. In 2008, we presented data at several scientific conferences on our TLR7 and TLR8 agonists.

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 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.

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Collaborative Alliances

Oncology Merck KGaA

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.

Under our agreement with Merck KGaA, Merck KGaA will determine how to proceed with further clinical development of IMO-2055 in the treatment of cancer. At present, we are conducting on behalf of Merck KGaA a clinical trial of IMO-2055 in combination with Avastin and Tarceva in patients with non-small cell lung cancer, and a clinical trial of IMO-2055 in combination with Erbitux and Camptosar in patients with colorectal cancer.

Non-small Cell Lung Cancer Avastin and Tarceva Combination Phase 1b Clinical 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 the safety of IMO-2055 in combination with standard dosages and schedules of Tarceva and Avastin and to determine the recommended dosage of IMO-2055 for potential use in a subsequent Phase 2 trial. 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. The initial three planned dose levels of IMO-2055 were well tolerated, and patients currently are being recruited at a fourth dose level for the trial, which was designed with a target enrollment of up to 40 patients.

Colorectal Cancer Erbitux and Camptosar Combination Phase 1b Clinical Trial. In February 2009, we began dosing the first patient in a Phase 1b clinical trial of 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 whose cancer had progressed during a prior course of standard therapy. The trial is designed to assess the safety of the IMO-2055, Erbitux, and Camptosar combination and to determine the recommended dosage of IMO-2055 for potential use in a subsequent Phase 2 clinical trial. Three dose levels of IMO-2055 are being investigated with standard dosages and schedules of Erbitux and Camptosar. IMO-2055 is administered subcutaneously once a week, with each patient continuing to receive therapy until disease progression as determined by RECIST or another protocol-specified stopping criterion is met. Patients currently are being recruited for the trial, which was designed with a target enrollment of up to 50 patients. We achieved a milestone under our agreement with Merck KGaA upon the dosing of the first patient in the Erbitux/Camptosar clinical trial.

Under our agreement with Merck KGaA, we have agreed with Merck KGaA that we will conduct, on its behalf, the on-going Phase 1b non-small cell lung cancer clinical trial and the on-going Phase 1b colorectal cancer clinical trial. We may initiate and conduct on behalf of Merck KGaA additional clinical trials of IMO-2055. Merck KGaA has agreed to reimburse us for costs associated with the two Phase 1b clinical trials incurred after February 4, 2008, which is the date our agreement with Merck KGaA became effective, and with any additional clinical trials that we may initiate and conduct.

We reported preliminary data from a Phase 2 Stage A clinical trial of IMO-2055 monotherapy in renal cell carcinoma in October 2008. The study contained four arms, comprised of treatment-naïve and second-line patients randomly assigned to receive IMO-2055 subcutaneously at either 0.16 mg/kg/week or 0.64 mg/kg/week. The primary objective of tumor response based on RECIST was not achieved in the study. Median progression-free survival for each of the four arms of the study was 2 months, 3 months, 4 months, and 4 months. IMO-2055 treatment was generally well-tolerated with good dose intensity in all arms of the study. We intend to present data from this clinical trial at a

scientific conference in the second half of 2009.

Prior to entering our collaboration with Merck KGaA, we conducted three previous Phase 1 clinical trials of IMO-2055. These studies included a rising dose trial in healthy volunteers, a rising dose trial in advanced cancer patients, and a combination trial of IMO-2055 with gemcitabine and carboplatin in advanced cancer patients.

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Vaccine Adjuvants Merck & Co.

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

In preclinical animal models, our TLR agonists have shown adjuvant activity when combined with various types of antigens. Preclinical studies that we 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. Merck & Co. is conducting preclinical studies to evaluate use of our TLR7, 8, and 9 agonists as vaccine adjuvants. In May 2008, we achieved a preclinical milestone under our collaboration with Merck & Co. involving one of our novel TLR9 agonists used as an adjuvant in cancer vaccines. In November 2008, Merck & Co. extended this research collaboration, which was originally for two years, for an additional year to December 2009.

Asthma and Allergies Novartis

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 that 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 September 2008, we achieved a milestone under our Novartis collaboration, related to the initiation of a Phase 1 clinical trial by Novartis of QAX935, a novel agonist of TLR9.

Collaborative Alliances

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

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;

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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.

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.

In February 2009, we amended the license agreement with Merck KGaA so that we could initiate and conduct on behalf of Merck KGaA additional clinical trials of IMO-2055, until such time as Merck has filed an IND application with the FDA and assumes sponsorship of these trials. Under the amendment, Merck KGaA has agreed to reimburse us for costs associated with any additional trials that we may initiate and conduct.

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. In November 2008, Merck & Co. extended this research collaboration for an additional one-year period to December 2009. 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;

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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 Merck & Co. s royalty obligation will terminate upon the achievement of a specified market share in such country by a competing vaccine containing an agonist targeting the same toll-like receptor as that targeted by the agonist in the Merck & Co. vaccine. In addition, the applicable royalties may be reduced if Merck & Co. is required to pay royalties to third parties for licenses to intellectual property rights, which royalties exceed a specified threshold. Merck & Co. s royalty and milestone obligations may also be reduced if Merck & Co. terminates the agreement based on specified uncured material breaches by us.

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

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. 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;

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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 initially 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 March 2008, the term of the research collaboration was further extended until December 31, 2008 in order to allow for QAX935, a novel TLR9 agonist, to be advanced into clinical trials prior to the end of the research and collaboration phase. Our research obligations under the agreement ended in the third quarter of 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 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. We are using our antisense expertise and technology to validate potential targets in the TLR signaling pathway, which may assist us in identifying drug candidates. We also believe that our antisense technology may be useful to pharmaceutical and biotechnology companies that are seeking to develop drug candidates that down-regulate gene targets discovered by, or proprietary to, such companies. Antisense drug candidates are designed to bind to RNA targets through hybridization, and decrease production of the specific protein encoded by the target RNA. We believe that drugs based on antisense technology may be more effective and cause fewer side effects than conventional drugs in applications with well-defined RNA targets because antisense drugs are designed to intervene in a highly specific fashion in the production of proteins, rather than after the proteins are made.

Currently, we are a party to four 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

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our patents and patent applications. Also under the agreement, we licensed from Isis specified antisense patents and patent applications, principally Isis suite of RNase H patents and patent applications. We also paid an initial licensing fee for this license and are obligated to pay Isis a maintenance fee and royalties. We have the right to use these patents and patent applications in our drug discovery and development efforts and in some types of third-party collaborations. The licenses granted under the Isis agreement terminate upon the last to expire of the patents and patent applications licensed under the agreement. We may terminate at any time the sublicense by Isis to us of the patents and patent applications.

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

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

Academic and Research Collaborations

We have entered into research collaborations with scientists at leading academic research institutions. These research collaborations allow us to augment our internal research capabilities and obtain access to specialized knowledge and expertise.

In general, our collaborative research agreements may require us to supply certain of our compounds and/or pay various amounts to support the research. Under these research agreements, if a collaborator, solely or jointly with us, creates any invention, we may own exclusively such invention or have an option to negotiate an exclusive, worldwide, royalty-bearing license to such invention. Inventions developed solely by our scientists in connection with research collaborations are owned exclusively by us. These collaborative agreements are non-exclusive and may be cancelled with limited notice.

Research and Development Expenses

For the years ended December 31, 2008, 2007 and 2006, we spent approximately $16.2 million, $13.2 million and $12.7 million, respectively, on research and development activities. In 2008, Merck KGaA sponsored approximately $1.4 million of our research and development activities. In 2008 and 2007, Merck & Co. sponsored approximately $1.5 million and $1.1 million, respectively, of our research and development activities. Our collaborators sponsored only a nominal portion of our research and development activities in 2006.

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,

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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 27, 2009, we owned 61 U.S. patents and U.S. patent applications and 204 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, IMO-2125, and IMO-3100.

To date, all of our intellectual property covering immune modulatory compositions and methods of their use is based on discoveries made solely by us. These patents expire at various dates ranging from 2017 to 2026.

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 27, 2009, our antisense patent portfolio included 107 U.S. patents and patent applications and 110 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.

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

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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.

In addition, the Food and Drug Administration Amendments Act of 2007, or FDAAA, granted significant new powers to the FDA, many of which are aimed at improving the safety of drug products before and after approval. In particular, FDAAA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information, and require risk evaluation and mitigation strategies for certain drugs, including certain currently approved drugs. It also significantly expands the federal government s clinical trial registry and results databank and creates new restrictions on the advertising and promotion of drug products. Under FDAAA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties, as well as other civil and 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, or GLP, 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 a 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 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 1b usually involves patients diagnosed with the disease or condition for which the study drug is intended and includes assessments compatible with the proposed mechanism of 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.

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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 and proposed labeling 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.

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

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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 other companies 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.

Competition

We are developing our TLR-targeted drug candidates for use in the treatment of infectious diseases, autoimmune and inflammatory 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.

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 an on-going Phase 1 clinical trial with a TLR9 agonist, SD-101, for hepatitis C treatment. Anadys Pharmaceutical, Inc., has an on-going Phase 1 clinical trial with ANA733, a TLR7 agonist prodrug, for hepatitis C treatment.

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In autoimmune diseases, Pfizer, Inc., has completed a Phase 1 clinical trial in healthy volunteers with a TLR antagonist, CPG 52364, for the treatment of lupus, and Dynavax Technologies Corporation with its collaborator, GlaxoSmithKline, is developing autoimmune and inflammatory disease therapeutics with their lead TLR inhibitor, DV1079.

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. Anadys Pharmaceutical, Inc., has announced that is has initiated a Phase 1 clinical trial in solid tumors for its TLR7 agonist prodrug ANA773. VentiRx Pharmaceuticals recently announced commencement of a Phase 1 clinical trial of VTX-2337, a TLR8 agonist for the treatment of cancer.

In asthma and allergies, Dynavax Technologies Corporation in collaboration with AstraZeneca Pharmaceuticals plc, is conducting preclinical studies of AZD1419, a TLR9 agonist for the treatment of asthma and COPD. Pfizer, Inc., in collaboration with sanofi-aventis Groupe has an ongoing Phase 1 clinical trial in asthma and allergic rhinitis with TLR9 agonist AVE-0675. Cytos Biotechnology has reported results from two Phase 2 clinical trials of its QbG10 technology platform, which includes TLR9 agonists in viral-like particles, in allergic rhinitis and has announced plans to initiate additional Phase 2b trials.

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 27, 2009, we employed 37 individuals full-time. Of our 37 employees, 24 are engaged in research and development and 20 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.

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.

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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 and 2008 when our recognition of revenues under license and collaboration agreements resulted in our reporting net income for those years. As of December 31, 2008, we had an accumulated deficit of $341.2 million. We have incurred losses of $81.0 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 will be sufficient to fund our operations at least through December 31, 2010.

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.

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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 collaborative alliances or through other means 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 or possibly relinquish rights to portions of our technology, drug candidates and/or products. 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 lead drug candidate for infectious diseases, IMO-2125, and our collaborative alliances. 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;
- 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.

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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. Moreover, companies developing drugs targeted to TLRs have experienced setbacks in clinical 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 HCV 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 HCV infection. Dynavax Technologies Corporation announced in March 2008 that two investigational new drug applications for its investigational hepatitis B vaccine, HEPLISAV, which includes a proprietary TLR9 agonist, had been placed on clinical hold by the FDA. Dynavax Technologies Corporation also announced in May 2008 discontinuation of the clinical development program for TOLAMBA ®, which comprises a TLR9 agonist covalently attached to ragweed antigen.

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 lower than we expect;
- 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;

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

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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 inadvertent, 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 clinical 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. In addition, in our Phase I clinical trial of IMO-2125 in patients with chronic HCV infection, due to the enrollment procedure, completion of each cohort has taken longer than anticipated. 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, including the pattern of patient enrollment;

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 Phase 1b clinical trial of IMO-2055 in oncology, and we commenced a Phase 1 clinical trial of IMO-2125 for chronic HCV infection. In 2008, our collaborator Novartis commenced a Phase 1 clinical trial of

QAX935, and in 2009 we commenced a second Phase 1b clinical trial of IMO-2055 under our collaboration with Merck KGaA. 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 clinical trials. Further, the chemical and pharmacological properties of RNA- and DNA-based compounds targeted to TLRs may not be fully recognized in preclinical studies 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, Dynavax Technologies announced in March 2008 that two investigational new drug applications for its investigational hepatitis B vaccine, HEPLISAV, which includes a proprietary TLR9 agonist, had been placed on clinical hold by the FDA. Dynavax Technologies also announced in May 2008 discontinuation of the clinical development program for TOLAMBA, which comprises a TLR9 agonist covalently attached to a ragweed antigen. In addition, Pfizer, Inc. and Anadys Pharmaceuticals, Inc. each have performed early clinical trials of TLR-targeted compounds for the treatment of chronic HCV 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 clinical trial. Pfizer, Inc., is conducting clinical trials of PF-3512676, a TLR9 agonist for treating cancer. In addition, Dynavax

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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 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 President, 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 400 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, 2011, 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 as part of our internal programs and IMO-2055 on behalf of Merck KGaA.

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 alliances 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, collaborations 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 alliances 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 collaborative alliances, 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 challenge our intellectual property rights or 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 alliance 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 collaborative alliances 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

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research collaboration 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. 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 collaborative alliances, 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 six 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 to pay a specified percentage of any sublicense income that we may receive. These licenses impose various commercialization, sublicensing, insurance and other obligations on us.

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Our failure to comply with these requirements could result in termination of the licenses. These licenses generally will otherwise remain in effect until the expiration of all valid claims of the patents covered by such licenses or upon earlier termination by the parties. The issued patents covered by these licenses expire at various dates ranging from 2014 to 2022. If one or more of these licenses is terminated, we may be delayed in our efforts, or be unable, to develop and market the products that are covered by the applicable license or licenses.

We may become involved in expensive patent litigation or other proceedings, which could result in our incurring substantial costs and expenses or substantial liability for damages or require us to stop our development and commercialization efforts.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the biotechnology industry. We may become a party to various types of patent litigation or other proceedings regarding intellectual property rights from time to time even under circumstances where we are not practicing and do not intend to practice any of the intellectual property involved in the proceedings. For instance, in 2002, 2003, and 2005, we became involved in interference proceedings declared by the United States Patent and Trademark Office for certain of our antisense and ribozyme patents. All of these interferences have since been resolved. We are neither practicing nor intending to practice the intellectual property that is associated with any of these interference proceedings.

The cost to us of any patent litigation or other proceeding even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If any patent litigation or other proceeding is resolved against us, we or our collaborators may be enjoined from developing, manufacturing, selling or importing our drugs without a license from the other party and we may be held liable for significant damages. We may not be able to obtain any required license on commercially acceptable terms or at all.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

Risks Relating to Product Manufacturing, Marketing and Sales and Reliance on Third Parties

Because we have limited manufacturing experience, facilities or infrastructure, we are dependent on third-party manufacturers to manufacture products for us. If we cannot rely on third-party manufacturers, we will be required to incur significant costs and devote significant efforts to establish our own manufacturing facilities and capabilities.

We have limited manufacturing experience and no manufacturing facilities, infrastructure or clinical or commercial scale manufacturing capabilities. In order to continue to develop our products, apply for regulatory approvals and ultimately commercialize products, we need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities.

We currently rely upon third parties to produce material for nonclinical, preclinical and clinical testing purposes and expect to continue to do so in the future. We also expect to rely upon third parties to produce materials that may be required for the commercial production of our products. Our current and anticipated future dependence upon others for the manufacture of our drug candidates may adversely affect our future profit margins and our ability to develop drug candidates and commercialize any drug candidates on a timely and competitive basis. We currently do not have any long term supply contracts and rely on only one contract manufacturer.

There are a limited number of manufacturers that operate under the FDA s cGMP regulations capable of manufacturing our products. As a result, we may have difficulty finding manufacturers for our products with adequate capacity for our needs. If we are unable to arrange for third-party manufacturing of our products on a timely basis, or to do so on commercially reasonable terms, we may not be able to complete development of our products or market them.

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Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control;
- the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us;
- the potential that third-party manufacturers will develop know-how owned by such third party in connection with the production of our products that is necessary for the manufacture of our products; and
- reliance upon third-party manufacturers to assist us in preventing inadvertent disclosure or theft of our proprietary knowledge.

Additionally, contract manufacturers may not be able to manufacture our TLR-targeted drug candidates at a cost or in quantities necessary to make them commercially viable. To date, our third-party manufacturers have met our manufacturing requirements, but we cannot be assured that they will continue to do so. Furthermore, changes in the manufacturing process or procedure, including a change in the location where the drug is manufactured or a change of a third-party manufacturer, may require prior FDA review and approval in accordance with the FDA s cGMP regulations. There are comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a product. The FDA or similar foreign regulatory agencies at any time may also implement new standards, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. If we or our contract manufacturers are unable to comply, we or they may be subject to regulatory action, civil actions or penalties.

We have no experience selling, marketing or distributing products and no internal capability to do so.

If we receive regulatory approval to commence commercial sales of any of our products, we will face competition with respect to commercial sales, marketing and distribution. These are areas in which we have no experience. To market any of our products directly, we would need to develop a marketing and sales force with technical expertise and with supporting distribution capability. In particular, we would need to recruit a large number of experienced marketing and sales personnel. Alternatively, we could engage a pharmaceutical or other healthcare company with an existing distribution system and direct sales force to assist us. However, to the extent we entered into such arrangements, we would be dependent on the efforts of third parties. If we are unable to establish sales and distribution capabilities, whether internally or in reliance on third parties, our business would suffer materially.

If third parties on whom we rely for clinical trials do not perform as contractually required or as we expect, we may not be able to obtain regulatory approval for or commercialize our products and our business may suffer.

We do not have the ability to independently conduct the clinical trials required to obtain regulatory approval for our products. We depend on independent clinical investigators, contract research organizations and other third-party service providers in the conduct of the clinical trials of our products and expect to continue to do so. We have contracted with contract research organizations to manage our current Phase 1 clinical trial of IMO-2125 in patients with chronic HCV infection. We rely heavily on these parties for successful execution of our clinical trials, but do not control many aspects of their activities. We are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply

with standards, commonly referred to as good clinical practices, for conducting, recording and reporting clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols. The failure of these third parties to carry out their obligations could delay or prevent the development, approval and

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commercialization of our products. If we seek to conduct any of these activities ourselves in the future, we will need to recruit appropriately trained personnel and add to our infrastructure.

The commercial success of any drug candidates that we may develop will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Any products that we ultimately bring to the market, if they receive marketing approval, may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the prevalence and severity of any side effects, including any limitations or warnings contained in the product s approved labeling;
- the efficacy and potential advantages over alternative treatments;
- the ability to offer our drug candidates for sale at competitive prices;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and the timing of market introduction of competitive products; and
- publicity concerning our products or competing products and treatments.

Even if a potential product displays a favorable efficacy and safety profile, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of our drug candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by conventional technologies marketed by our competitors.

If we are unable to obtain adequate reimbursement from third-party payors for any products that we may develop or acceptable prices for those products, our revenues and prospects for profitability will suffer.

Most patients rely on Medicare, Medicaid, private health insurers, and other third-party payors to pay for their medical needs, including any drugs we may market. If third-party payors do not provide adequate coverage or reimbursement for any products that we may develop, our revenues and prospects for profitability will suffer. Congress enacted a limited prescription drug benefit for Medicare recipients in the Medicare Prescription Drug and Modernization Act of 2003. While the program established by this statute may increase demand for our products, if we participate in this program, our prices will be negotiated with drug procurement organizations for Medicare beneficiaries and are likely to be lower than we might otherwise obtain. Non-Medicare third-party drug procurement organizations may also base the price they are willing to pay on the rate paid by drug procurement organizations for Medicare beneficiaries.

A primary trend in the United States healthcare industry is toward cost containment. In addition, in some foreign countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to

governmental control. In these countries, pricing negotiations with governmental authorities can take six months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our drug candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization of our products. These further clinical trials would require additional time, resources and expenses. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our prospects for generating revenue, if any, could be adversely affected and our business may suffer.

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Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved healthcare products. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we may develop. Cost control initiatives could decrease the price we might establish for products that we may develop, which would result in lower product revenues to us.

We face a risk of product liability claims and may not be able to obtain insurance.

Our business exposes us to the risk of product liability claims that is inherent in the manufacturing, testing and marketing of human therapeutic drugs. We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and will face an even greater risk if we commercially sell any products. Regardless of merit or eventual outcome, liability claims and product recalls may result in:

decreased demand for our drug candidates and products;

damage to our reputation;

regulatory investigations that could require costly recalls or product modifications;

withdrawal of clinical trial participants;

costs to defend related litigation;

substantial monetary awards to clinical trial participants or patients, including awards that substantially exceed our product liability insurance, which we would then have to pay using other sources, if available, and would damage our ability to obtain liability insurance at reasonable costs, or at all, in the future;

loss of revenue;

the diversion of management s attention away from managing our business; and

the inability to commercialize any products that we may develop.

Although we have product liability and clinical trial liability insurance that we believe is adequate, this insurance is subject to deductibles and coverage limitations. We may not be able to obtain or maintain adequate protection against potential liabilities. If we are unable to obtain insurance at acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which may materially and adversely affect our business and financial position. These liabilities could prevent or interfere with our commercialization efforts.

Risks Relating to an Investment in Our Common Stock

Our corporate governance structure, including provisions in our certificate of incorporation and by-laws, our stockholder rights plan and Delaware law, may prevent a change in control or management that stockholders may consider desirable.

Section 203 of the Delaware General Corporation Law and our certificate of incorporation, by-laws, and stockholder rights plan contain provisions that might enable our management to resist a takeover of our company or discourage a third party from attempting to take over our company. These provisions include:

a classified board of directors,

limitations on the removal of directors,

limitations on stockholder proposals at meetings of stockholders,

the inability of stockholders to act by written consent or to call special meetings, and

the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval.

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In addition, Section 203 of the Delaware General Corporation Law imposes restrictions on our ability to engage in business combinations and other specified transactions with significant stockholders. These provisions could have the effect of delaying, deferring, or preventing a change in control of us or a change in our management that stockholders may consider favorable or beneficial. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock.

Our stock price has been and may in the future be extremely volatile. In addition, because an active trading market for our common stock has not developed, our investors ability to trade our common stock may be limited. As a result, investors may lose all or a significant portion of their investment.

Our stock price has been volatile. During the period from January 1, 2007 to March 9, 2009, the closing sales price of our common stock ranged from a high of $15.41 per share to a low of $4.66 per share. The stock market has also experienced significant price and volume fluctuations, particularly within the past year, and the market prices of biotechnology companies in particular have been highly volatile, often for reasons that have been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

results of clinical trials of our drug candidates or those of our competitors;

the regulatory status of our drug candidates;

failure of any of our drug candidates, if approved, to achieve commercial success;

the success of competitive products or technologies;

regulatory developments in the United States and foreign countries;

our success in entering into collaborative agreements;

developments or disputes concerning patents or other proprietary rights;

the departure of key personnel;

variations in our financial results or those of companies that are perceived to be similar to us;

our cash resources;

the terms of any financing conducted by us;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts reports or recommendations; and

general economic, industry and market conditions.

In addition, our common stock has historically been traded at low volume levels and may continue to trade at low volume levels. As a result, any large purchase or sale of our common stock could have a significant impact on the price of our common stock and it may be difficult for investors to sell our common stock in the market without depressing the market price for the common stock or at all.

As a result of the foregoing, investors may not be able to resell their shares at or above the price they paid for such shares. Investors in our common stock must be willing to bear the risk of fluctuations in the price of our common stock and the risk that the value of their investment in our stock could decline.

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

None.

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Item 2. ***Properties***

We lease approximately 26,000 square feet of laboratory and office space located in Cambridge, Massachusetts. The lease expires on May 31, 2014 and we have specified rights to sublease this facility and a five-year renewal option.

Item 3. ***Legal Proceedings***

None.

Item 4. ***Submission of Matters to a Vote of Security Holders***

None.

Executive Officers of Idera Pharmaceuticals

The following table sets forth the names, ages and positions of our executive officers as of March 1, 2009:

Name	Age	Position
Sudhir Agrawal, D. Phil	55	President, Chief Executive Officer, Chief Scientific Officer and Director
Louis J. Arcudi, III	48	Chief Financial Officer, Treasurer and Secretary
Alice S. Bexon, MBChB	39	Vice President of Clinical Development
Timothy M. Sullivan, Ph.D	54	Vice President of Development Programs

Sudhir Agrawal, D. Phil., is our President, Chief Executive Officer and Chief Scientific Officer. He joined us in 1990 and has served as our Chief Scientific Officer since January 1993, our Senior Vice President of Discovery since March 1994, our President from February 2000 to October 2005 and since September 2008, a director since March 1993 and our Chief Executive Officer since August 2004. Prior to his appointment as Chief Scientific Officer, he served as our Principal Research Scientist from February 1990 to January 1993 and as our Vice President of Discovery from December 1991 to January 1993. He served as Acting Chief Executive Officer from February 2000 until September 2001. Prior to joining us, Dr. Agrawal served as a Foundation Scholar at the Worcester Foundation for Experimental Biology from 1987 through 1991 and at the Medical Research Council s Laboratory of Molecular Biology in Cambridge, England from 1985 to 1986. Dr. Agrawal received a D. Phil. in chemistry in 1980 from Allahabad University in India. He has authored more than 290 research papers and reviews. He is a member of the editorial board of several scientific journals. Dr. Agrawal is co-author of more than 400 patents and patent applications worldwide.

Louis J. Arcudi, III is our Chief Financial Officer, Treasurer and Secretary. He joined us in December 2007. Prior to joining us, Mr. Arcudi served as Vice President of Finance and Administration and Treasurer for Peptimmune, Inc., a biotechnology company, from 2003 to 2007. From 2000 to 2003 Mr. Arcudi was Senior Director of Finance and Administration at Genzyme Molecular Oncology Corporation, a division of Genzyme Corporation, a biotechnology company. He was Director of Finance Business Planning and Operations International at Genzyme Corporation from 1998 to 2000. Prior to joining Genzyme, he held finance positions with increasing levels of responsibility at Cognex Corporation, a supplier of machine vision systems, Millipore Corporation, a provider of technologies, tools and services for bioscience, research and biopharmaceutical manufacturing, and General Motors Corporation, an automobile manufacturer. Mr. Arcudi received a M.B.A. from Bryant College and a B.S. in accounting and information systems from the University of Southern New Hampshire.

Alice S. Bexon, MBChB, joined us in January 2007 as our Vice President of Clinical Development. From April 2001 to January 2007, Dr. Bexon worked for Hoffmann-La Roche, Inc. s Pharma Division, where she served initially as International Medical Leader for the Oncology Business organization from April 2001 through June 2006 and subsequently as Clinical Science Leader for Pharma Development Medical Oncology from July 2006 to January 2007. Dr. Bexon also served as Medical Director from 1998 to 2001 in the oncology business unit of Sanofi-Synthelabo s French affiliate (now sanofi-aventis), a pharmaceutical company. In addition,

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from 1997 to 1998 Dr. Bexon worked for the European Organization for Research and Treatment of Cancer (subsequently NDDO Oncology) in the Netherlands, and in 1997, she worked for Parexel International, a global bio/pharmaceutical services organization, in France. Dr. Bexon received her MBChB (MD equivalent) from Bristol University Medical School in the United Kingdom in 1994 and her full General Medical Council registration to practice medicine the following year. She completed internships in internal medicine and general surgery at Newcastle s Freeman and North Tyneside General Hospitals in the UK and her oncology residency under Professor Jean-Pierre Armand at the Institut Gustave Roussy in Villejuif, France.

Timothy M. Sullivan, Ph.D., has been our Vice President of Development Programs since August 2004. He joined us in 2002 as Senior Director, Preclinical Drug Development. His prior professional experience includes positions as Executive Director of Non-clinical Drug Safety Evaluation for Purdue Pharma L.P., a pharmaceutical company, from 1999 to 2002 and Vice President of Eastern Operations for Oread, Inc., a contract drug development organization, from 1997 to 1999. Prior to 1997, Dr. Sullivan held a variety of technical management roles with other pharmaceutical companies and contract research organizations (Adria, Battelle, Roma Toxicology Centre), and in veterinary medicine (International Minerals & Chemical). Dr. Sullivan earned his B.S. in microbiology from Michigan State University in 1975. His graduate studies were at Purdue University, where he earned a M.S. degree in health physics in 1978 and a Ph.D. in toxicology in 1981.

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PART II.

Item 5. ***Market For Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Market Information

Our common stock has been listed on the NASDAQ Global Market under the symbol IDRA since December 10, 2007. Prior to December 10, 2007, our common stock was listed on the American Stock Exchange under the symbol IDP.

The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock during each of the quarters set forth below as reported on the NASDAQ Global Market. These prices reflect inter-dealer prices without retail mark-up, mark-down or commission and may not necessarily represent actual transactions.

	High	Low
2007		
First Quarter	$ 9.50	$ 5.22
Second Quarter	9.95	6.25
Third Quarter	9.22	6.21
Fourth Quarter	13.10	8.86
2008		
First Quarter	$ 13.60	$ 7.65
Second Quarter	15.60	9.88
Third Quarter	15.40	10.90
Fourth Quarter	14.50	5.59

As of February 27, 2009, we had approximately 240 common stockholders of record.

Dividends

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future.

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Item 6. ***Selected Financial Data***

The following selected financial data are derived from our financial statements. The data should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and the financial statements, related notes, and other financial information included herein.

	Year Ended December 31,				
	2008	2007	2006	2005	2004
	(In thousands, except per share data)				
Statement of Operations Data:					
Alliance revenue	$ 26,376	$ 7,981	$ 2,421	$ 2,467	$ 942
Operating expenses:					
Research and development	16,152	13,195	12,705	11,170	8,249
General and administrative	9,724	9,513	6,276	5,120	5,616
Total operating expenses	25,876	22,708	18,981	16,290	13,865
Income (loss) from operations	500	(14,727)	(16,560)	(13,823)	(12,923)
Other income (expense):					
Investment income, net	1,344	1,668	505	369	217
Interest expense	(92)	(149)	(425)	(252)	(29)
Foreign currency exchange loss	(267)				
Income (loss) before income taxes	1,485	(13,208)	(16,480)	(13,706)	(12,735)
Income tax benefit (provision)	24		(45)		
Net income (loss)	1,509	(13,208)	(16,525)	(13,706)	(12,735)
Accretion of preferred stock dividends					(2,676)
Net income (loss) applicable to common stockholders	$ 1,509	$ (13,208)	$ (16,525)	$ (13,706)	$ (15,411)
Basic net income (loss) per share	$ 0.07	$ (0.62)	$ (0.99)	$ (0.99)	$ (1.03)
Accretion of preferred stock					(0.22)
Net income (loss) per share applicable to common stockholders	$ 0.07	$ (0.62)	$ (0.99)	$ (0.99)	$ (1.25)
Diluted net income (loss) per share	$ 0.06	$ (0.62)	$ (0.99)	$ (0.99)	$ (1.03)
Accretion of preferred stock dividends					(0.22)
Net income (loss) per share applicable to common stockholders	$ 0.06	$ (0.62)	$ (0.99)	$ (0.99)	$ (1.25)
Shares used in computing basic net income (loss) per common share(1)	22,655	21,221	16,625	13,886	12,364

Shares used in computing diluted net income (loss) per common share(1)	25,331	21,221	16,625	13,886	12,364
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 55,606	$ 23,743	$ 38,187	$ 8,376	$ 14,413
Working capital	32,099	15,908	30,984	4,998	13,181
Total assets	59,400	27,714	40,541	9,989	15,391
Capital lease obligations	49	70	10	17	
Note payable		1,143			
4% convertible subordinated notes payable			5,033	5,033	
Accumulated deficit	(341,225)	(342,734)	(329,526)	(313,000)	(299,294)
Total stockholders equity (deficit)	22,167	7,719	12,237	(335)	12,769

(1) Computed on the basis described in Note 13 of notes to financial statements appearing elsewhere in this Annual Report on Form 10-K.

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

Overview

We are engaged in the discovery and development of DNA- and RNA-based drug candidates targeted to Toll-Like Receptors, or TLRs, to treat infectious diseases, autoimmune and inflammatory diseases, cancer, and asthma and allergies, and for usmily:Times New Roman,Times,serif;font-size: 7pt;">

J. Taylor Crandall*

Chairman

Charles R. Cummings*

Chairman

Hill A. Feinberg

Gerald J. Ford

Jeremy B. Ford

J. Markham Green*

William T. Hill, Jr.*

James Huffines

Lee Lewis

Andrew J. Littlefair*

W. Robert Nichols, III*

Chairman

C. Clifton Robinson

Kenneth D. Russell

Chairman

A. Haag Sherman*

Chairman

Robert C. Taylor, Jr.*

Carl B. Webb

Alan B. White

Chairman

Meetings in Fiscal 2015

8

5

4

7

5

0

9

* Denotes independent director.

Audit Committee

We have a standing Audit Committee established within the meaning of Section 3(a)(58)(A) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The Audit Committee helps our Board of Directors ensure the integrity of our financial statements, the qualifications and independence of our independent registered public accounting firm and the performance of our internal audit function and independent registered public accounting firm. In furtherance of those matters, the Audit Committee assists in the establishment and maintenance of our internal audit controls, selects, meets with and assists the independent registered public accounting firm, oversees each annual audit and quarterly review and prepares the report that federal securities laws require be included in our annual proxy statement, which appears on page 56. Mr. Cummings has been designated as Chairman, and Messrs. Green and Bolt are members, of the Audit Committee. Our Board of Directors has reviewed the education, experience and other qualifications of each member of the Audit Committee. Based upon that review, our Board of Directors has determined that each of Mr. Cummings and Mr. Bolt qualifies as an “audit committee financial expert,” as defined by the rules of the SEC, and each member of the Audit Committee is independent in accordance with the listing standards of the NYSE. Currently, none of our Audit Committee members serve on the audit committees of three or more public companies.

Compensation Committee

The Compensation Committee reviews and approves the compensation and benefits of our executive officers, administers the Hilltop Holdings Inc. 2012 Annual Incentive Plan, or the Annual Incentive Plan, the Hilltop Holdings Inc. 2003 Equity Incentive Plan, or the 2003 Equity Incentive Plan, and the Hilltop Holdings Inc. 2012 Equity Incentive Plan, or the 2012 Equity Incentive Plan, and produces the annual report on executive compensation for inclusion in our annual proxy statement, which appears on page 40. Each member is independent in accordance with the listing standards of the NYSE.

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Nominating and Corporate Governance Committee

The Nominating and Corporate Governance Committee's purpose is as follows:

- Identify, screen and recommend to our Board of Directors individuals qualified to serve as members, and on committees, of the Board of Directors;
- Advise our Board of Directors with respect to the composition, procedures and committees of the Board of Directors;
- Advise our Board of Directors with respect to the corporate governance principles applicable to the Company; and
- Oversee the evaluation of the Board of Directors and our management.

Each member of the Nominating and Corporate Governance Committee is independent in accordance with the listing standards of the NYSE.

Risk Committee

The purpose of the Risk Committee is to provide assistance to the Board of Directors in its oversight of:

- The Company's risk governance structure;
- The Company's risk tolerance;
- The Company's risk management and risk assessment guidelines and policies regarding market, credit, operation, liquidity, funding, reputational, regulatory, and such other risks as necessary;
- The Company's capital and liquidity and funding; and
- The performance of the Company's Chief Risk Officer.

The duties assigned to the Risk Committee are meant to ensure that there is an effective system reasonably designed to evaluate and control risk throughout the Company.

Investment Committee

The Investment Committee is responsible for, among other things, reviewing investment policies, strategies and programs; reviewing the procedures that we utilize in determining that funds are invested in accordance with policies

and limits approved by the Investment Committee; and reviewing the quality and performance of our investment portfolios and the alignment of asset duration to liabilities.

Merger and Acquisition Committee

The purpose of the Merger and Acquisition Committee is to review potential mergers, acquisitions or dispositions of material assets or a material portion of any business proposed by management and to report its findings and conclusions to the Board of Directors. Each member of the Merger and Acquisition Committee is independent in accordance with the listing standards of the NYSE.

Executive Committee

The Executive Committee, with certain exceptions, has the power and authority of the Board of Directors to manage the affairs of the Company between meetings of the Board of Directors.

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Corporate Governance

General

We are committed to good corporate governance practices and, as such, we have adopted formal corporate governance guidelines to maintain our effectiveness. The guidelines govern, among other things, board member qualifications, responsibilities, education, management succession and executive sessions. A copy of the corporate governance guidelines may be found at our corporate website at ir.hilltop-holdings.com under the heading “Investor Relations — Corporate Information — Governance Documents.” A copy also may be obtained upon request from our corporate Secretary at the address listed under “Questions” on page 58.

Board Leadership Structure

We have separated the offices of Chief Executive Officer and Chairman of the Board as a means of separating management of the Company from our Board of Director’s oversight of management. Separating these roles also enables an orderly leadership transition when necessary. We believe, at this time, that this structure provides desirable oversight of our management and affairs. We have in the past appointed, and will continue to appoint, lead independent directors as circumstances require.

Risk Oversight

Our Board of Directors and the Risk Committee of the Board of Directors oversee an enterprise-wide approach to risk management, intended to support the achievement of organizational objectives, including strategic objectives, to improve long-term organizational performance and enhance stockholder value. Our Board of Directors and the Risk Committee are actively involved in establishing and refining our business strategy, including assessing management’s appetite for risk and determining the appropriate level of overall risk for the Company. The Company conducts continual assessments through the Chief Risk Officer who is overseen by the Risk Committee.

While the Board of Directors has the ultimate oversight responsibility for the risk management process, various committees of the Board of Directors outside of the Risk Committee also have responsibility for risk management. In particular, the Audit Committee focuses on financial risk, including internal controls, and, from time to time, discusses and evaluates matters of risk, risk assessment and risk management with our management team. The Compensation Committee is responsible for overseeing the management of risk associated with our compensation policies and arrangements. The Nominating and Corporate Governance Committee ensures that the internal rule processes by which we are governed are consistent with prevailing governance practices and applicable laws and regulations.

Finally, the Investment Committee ensures that our funds are invested in accordance with policies and limits approved by it. Our Senior Officer Code of Ethics, General Code of Ethics and Business Conduct, committee charters and other governance documents are reviewed by the appropriate committees annually to confirm continued compliance, ensure that the totality of our risk management processes and procedures is appropriately comprehensive and effective and that those processes and procedures reflect established best practices.

Board Performance

Our Board of Directors conducts a survey of its members regarding its performance and reviews the results of the survey with a view to improving efficacy and effectiveness of the Board of Directors. In addition, the full Board of Directors reviews annually the qualifications and effectiveness of the Audit Committee and its members.

Director Qualifications for Service

As described below, the Nominating and Corporate Governance Committee considers a variety of factors when evaluating a potential candidate to fill a vacancy on the Board of Directors or when nomination of an incumbent director for re-election is under consideration. The Nominating and Corporate Governance Committee and the Board of Directors strive to balance a diverse mix of experience, perspective, skill and background with the practical requirement that the Board of Directors will operate collegially, with the common purpose of overseeing our business on behalf of our stockholders. All of our directors possess relevant experience, and each of them approaches the business of the Board of

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Directors and their responsibilities with great seriousness of purpose. The following describes, with respect to each director, his or her particular experience, qualifications, attributes and skills that qualify him or her to serve as a director:

Charlotte Jones Anderson	Ms. Anderson has significant managerial and executive officer experience with large entrepreneurial businesses and provides the Board of Directors the perspective of one of PlainsCapital's significant customers.
Rhodes Bobbitt	Mr. Bobbitt has an extensive investment background. This is particularly important given our available cash on hand and the investment portfolios at our subsidiaries.
Tracy A. Bolt	Mr. Bolt has significant experience concerning accounting matters that is essential to our Audit Committee's and Board of Directors' oversight responsibilities.
W. Joris Brinkerhoff	Mr. Brinkerhoff has participated, and continues to participate, in a number of business interests. Accordingly, he brings knowledge and additional perspectives to our Board of Directors from experiences with those interests.
J. Taylor Crandall	Mr. Crandall has significant experience in finance and management and board governance, including his experience serving on the Boards of Directors of several public and private companies.
Charles R. Cummings	Mr. Cummings has an extensive operational and accounting background. His expertise in these matters brings considerable strength to our Audit Committee and Board of Directors in these areas.
Hill A. Feinberg	Mr. Feinberg has extensive knowledge and experience concerning the broker-dealer segment and the industry in which it operates through his extended period of service to First Southwest and Hilltop Securities.
Gerald J. Ford	Mr. Gerald J. Ford has been a financial institutions entrepreneur and private investor involved in numerous mergers and acquisitions of private and public sector financial institutions over the past 40 years. His extensive banking industry experience and educational background provide him with significant knowledge in dealing with financial and regulatory matters, making him a valuable member of our Board of Directors. In addition, his service on the boards of directors and audit and corporate governance committees of a variety of public companies gives him a deep understanding of the role of the Board of Directors.
Jeremy B. Ford	Mr. Jeremy B. Ford's career has focused on mergers and acquisitions in the financial services industry. Accordingly, he has been actively involved in numerous acquisitions, including our acquisitions of NLC, PlainsCapital, substantially all of the assets of FNB, and SWS. His extensive knowledge of our operations makes him a valuable member of our Board of Directors.
J. Markham Green	Mr. Green has an extensive background in financial services, as well as board service. His investment banking background also provides our Board of Directors with expertise surrounding acquisitions and investments.

William T. Hill, Jr.	Mr. Hill's experience with legal and compliance matters, along with his management of a large group of highly skilled professionals, have given him considerable knowledge concerning many matters that come before our Board of Directors. Mr. Hill has also served on several civic and charitable boards, which has given him invaluable experience in corporate governance matters.
James R. Huffines	Mr. Huffines' significant banking and managerial experience provide unique insights and experience to our Board of Directors.

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Lee Lewis	Through his service on our Board of Directors and PlainsCapital's Board of Directors, Mr. Lewis has many years of knowledge of PlainsCapital and the challenges and opportunities that it is presented. The background of Mr. Lewis as an owner and chief executive officer of a Texas-based company also provides unique insight to the Board of Directors.
Andrew J. Littlefair	Mr. Littlefair has significant experience serving as a chief executive officer and as a director of publicly traded companies and provides the Board of Directors with the perspective of one of PlainsCapital's significant customers.
W. Robert Nichols III	Mr. Nichols has broad experience in managing and leading enterprises. This significant experience provides our Board of Directors with additional perspectives on our operations.
C. Clifton Robinson	Mr. Robinson possesses particular knowledge and experience in the insurance industry, as we purchased NLC from him in 2007. Mr. Robinson provides our Board of Directors with expertise in regards to our insurance operations.
Kenneth D. Russell	Mr. Russell's extensive background in accounting and operating entities provides valuable insight to our Board of Directors, including merger and acquisition activities.
A. Haag Sherman	Mr. Sherman has significant experience concerning investing, legal and accounting matters that is essential to our Board of Director's oversight responsibilities.
Robert C. Taylor, Jr.	Through his service on our Board of Directors and PlainsCapital's Board of Directors, Mr. Taylor has many years of knowledge of PlainsCapital and the challenges and opportunities that it is presented. The background of Mr. Taylor as a manager of a Texas-based company also provides unique insight to the Board of Directors.
Carl B. Webb	Mr. Webb possesses particular knowledge and experience in strategic planning and the financial industry, as well as expertise in finance, that strengthen the Board of Directors' collective qualifications, skills and experience.
Alan B. White	Mr. White possesses knowledge of our business and industry through his lengthy tenure as PlainsCapital's Chief Executive Officer that aids him in efficiently and effectively identifying and executing our strategic priorities.

Executive Board Sessions

The current practice of our Board of Directors is to hold an executive session of its non-management directors at least once per quarter. The individual who serves as the chair at these executive sessions is the Chairman of the Board of Directors. Executive sessions of the independent directors of the Board of Directors also are held at least once per fiscal year, and the independent directors select the independent director to preside over each executive session.

Communications with Directors

Our Board of Directors has established a process to receive communications from stockholders and other interested parties. Stockholders and other interested parties may contact any member or all members of the Board of Directors by mail. To communicate with our Board of Directors, any individual director or any group or committee of directors, correspondence should be addressed to the Board of Directors or any such individual director or group or committee of directors by either name or title. The correspondence should be sent to Hilltop Holdings Inc., c/o Secretary, 200 Crescent Court, Suite 1330, Dallas, Texas 75201.

All communications received as set forth in the preceding paragraph will be opened by the office of our General Counsel for the sole purpose of determining whether the contents represent a message to our directors. Any contents that are not in the nature of advertising, promotions of a product or service or patently offensive material will be forwarded

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promptly to the addressee(s). In the case of communications to the Board of Directors or any group or committee of directors, the General Counsel's office will make sufficient copies of the contents to send to each director who is a member of the group or committee to whom the communication is addressed. If the amount of correspondence received through the foregoing process becomes excessive, our Board of Directors may consider approving a process for review, organization and screening of the correspondence by the corporate Secretary or other appropriate person.

Code of Business Conduct and Ethics

We have adopted a Senior Officer Code of Ethics applicable to our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer. We also have adopted a General Code of Ethics and Business Conduct applicable to all officers, directors and employees. Both codes are available on our website at ir.hilltop-holdings.com under the heading "Investor Relations — Corporate Information — Governance Documents." Copies also may be obtained upon request by writing our corporate Secretary at the address listed under "Questions" on page 58. We intend to disclose any amendments to, or waivers from, our Senior Officer Code of Ethics and our General Code of Ethics and Business Conduct at the same website address provided above.

Director Nomination Procedures

The Nominating and Corporate Governance Committee believes that, at a minimum, candidates for membership on the Board of Directors should have a demonstrated ability to make a meaningful contribution to the Board of Directors' oversight of our business and affairs and have a record and reputation for honest and ethical conduct. The Nominating and Corporate Governance Committee recommends director nominees to the Board of Directors based on, among other things, its evaluation of a candidate's experience, knowledge, skills, expertise, integrity, ability to make independent analytical inquiries, understanding of our business environment and a willingness to devote adequate time and effort to board responsibilities. In making its recommendations to the Board of Directors, the Nominating and Corporate Governance Committee also seeks to have the Board of Directors nominate candidates who have diverse backgrounds and areas of expertise so that each member can offer a unique and valuable perspective.

The Nominating and Corporate Governance Committee expects, in the future, to identify potential nominees by asking current directors and executive officers to notify the committee if they become aware of persons who meet the criteria described above. The Nominating and Corporate Governance Committee also, from time to time, may engage firms, at our expense, that specialize in identifying director candidates. As described below, the Nominating and Corporate Governance Committee also will consider candidates recommended by stockholders.

Once a person has been identified by the Nominating and Corporate Governance Committee as a potential candidate, the committee expects to collect and review publicly available information regarding the person to assess whether the person should be considered further. If the Nominating and Corporate Governance Committee determines that the

candidate warrants further consideration, and if the person expresses a willingness to be considered and to serve on the Board of Directors, the Nominating and Corporate Governance Committee expects to request information from the candidate, review the person's accomplishments and qualifications, including in light of any other candidates that the committee might be considering, and conduct one or more interviews with the candidate. In certain instances, members of the Nominating and Corporate Governance Committee may contact one or more references provided by the candidate or may contact other members of the business community or other persons that may have greater first-hand knowledge of the candidate's accomplishments.

In addition to formally nominating individuals for election as directors in accordance with our Second Amended and Restated Bylaws, as summarized below on page 58 under "Stockholder Proposals for 2017," stockholders may send written recommendations of potential director candidates to the Nominating and Corporate Governance Committee for its consideration. Such recommendations should be submitted to the Nominating and Corporate Governance Committee "c/o Secretary" at Hilltop Holdings Inc., 200 Crescent Court, Suite 1330, Dallas, Texas 75201. Director recommendations submitted by stockholders should include the following information regarding the stockholder making the recommendation and the individual(s) recommended for nomination:

· name, age, business address and residence address;

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- the class, series and number of any shares of Hilltop stock or other securities of Hilltop or any affiliate of Hilltop owned, beneficially or of record (including the name of the nominee holder if beneficially owned);
- the date(s) that shares of Hilltop stock or other securities of Hilltop or any affiliate of Hilltop were acquired and the investment intent of such acquisition;
- any short interest (including any opportunity to profit or share in any benefit from any decrease in the price of such stock or other security) in any securities of Hilltop or any affiliate of Hilltop;
- whether and the extent to which such person, directly or indirectly (through brokers, nominees or otherwise), is subject to or during the prior six months has engaged in, any hedging, derivative or other transaction or series of transactions or entered into any other agreement, arrangement or understanding (including any short interest, any borrowing or lending of securities or any proxy or voting agreement), the effect or intent of which is to (a) manage risk or benefit of changes in the price of Hilltop securities or any security of any entity listed in the peer group in the stock performance graph included in the materials distributed with this Proxy Statement or (b) increase or decrease the voting power of such person in Hilltop disproportionately to such person's economic interest in Hilltop securities (or, as applicable, any security of any entity listed in the peer group in the stock performance graph included in the materials distributed with this Proxy Statement);
- any substantial interest, direct or indirect (including, without limitation, any existing or prospective commercial, business or contractual relationship with us), by security holdings or otherwise of such person in us or in any of our affiliates, other than an interest arising from the ownership of securities where such person receives no extra or special benefit not shared on a pro rata basis by all other holders of the same class or series;
- the investment strategy or objective, if any, of the stockholder making the recommendation and a copy of the prospectus, offering memorandum or similar document, if any, provided to investors, or potential investors, in such stockholder (if not an individual);
- to the extent known by the stockholder making the recommendation, the name and address of any other stockholder supporting the nominee for election or reelection as a director;
- a certificate executed by the proposed nominee that certifies that the proposed nominee is not, and will not, become a party to any agreement, arrangement or understanding with any person or entity other than us in connection with service or action as a director that has not been disclosed to us and that the proposed nominee consents to being named in a proxy statement and will serve as a director if elected;
- completed proposed nominee questionnaire (which will be provided upon request by writing or telephoning our corporate Secretary at the address or phone number listed under "Questions" on page 58); and
- all other information that would be required to be disclosed in solicitations of proxies for election of directors in an election contest, or is otherwise required, in each case pursuant to Regulation 14A under the Exchange Act and the rules promulgated thereunder.

The stockholder recommendation and information described above must be delivered to the corporate Secretary not earlier than the 120th day and not later than 5:00 p.m., Dallas, Texas local time, on the 90th day prior to the first anniversary of the date of the proxy statement for the preceding year's annual meeting of stockholders; provided, however, that if the date of the annual meeting is advanced more than 30 days prior to, or delayed by more than 30 days after, the first anniversary of the date of the preceding year's annual meeting, the stockholder recommendation and information must be delivered not earlier than the 120th day prior to the date of such annual meeting and not later than 5:00 p.m., Dallas, Texas local time, on the later of the 90th day prior to the date of such annual meeting of stockholders and the 10th day following the date on which public announcement of the date of such annual meeting is first made. In the event, however, the number of directors to be elected to the Board of Directors is increased and there is no public announcement of such action at least 100 days prior to the first anniversary of the date of the proxy statement for the preceding year's annual meeting, a stockholder recommendation also will be considered timely, but only with respect to nominees for any new positions created by the increase, if it is delivered to the corporate Secretary not later than 5:00 p.m., Dallas, Texas local time, on the 10th day following the day on which the public announcement is first made.

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The Nominating and Corporate Governance Committee expects to use a similar process to evaluate candidates to the Board of Directors recommended by stockholders as the one it uses to evaluate candidates otherwise identified by the committee.

No fee was paid to any third party or parties to identify or evaluate, or assist in identifying or evaluating, potential nominees.

The Nominating and Corporate Governance Committee did not receive the name of any stockholder recommendations for director nominees with respect to the Annual Meeting.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

Principal Stockholders

The following table sets forth information regarding our common stock beneficially owned on April 21, 2016 by any person or "group," as that term is used in Section 13(d)(3) of the Exchange Act, known to us to beneficially own more than five percent of the outstanding shares of our common stock.

Name and Address of Beneficial Owner	Amount and Nature of Beneficial Ownership	Percent of Class (a)	
Gerald J. Ford (b) 200 Crescent Court, Suite 1350 Dallas, Texas 75201	15,560,490	15.8	%
Wellington Management Group LLP (c) c/o Wellington Management Company LLP 280 Congress Street Boston, Massachusetts 02210	5,509,936	5.6	%
The Vanguard Group Inc. (d) 100 Vanguard Boulevard Malvern, Pennsylvania 19355	5,411,570	5.5	%

(a)

Based on 98,498,077 shares of common stock outstanding on April 21, 2016. Shares issuable under instruments to purchase our common stock that are exercisable within 60 days of April 21, 2016 are treated as if outstanding for computing the percentage ownership of the person holding these instruments, but are not treated as outstanding for purposes of computing the percentage ownership of any other person.

(b) The shares of common stock beneficially owned by Mr. Gerald J. Ford include 7,950 shares that are owned by Turtle Creek Revocable Trust, a revocable trust for the benefit of the members of Mr. Gerald J. Ford's family, and indirectly by Mr. Gerald J. Ford as settlor of the trust. Mr. Gerald J. Ford disclaims beneficial ownership of the shares held by the trust except to the extent of his pecuniary interest therein. Also includes 15,544,674 shares owned by Diamond A Financial, LP. Mr. Gerald J. Ford is the sole general partner of Diamond A Financial, LP. Mr. Gerald J. Ford has sole voting and dispositive power of these shares. Excludes 60,000 restricted stock units ("RSUs") that will not vest within 60 days of April 21, 2016.

(c) Based on the Schedule 13G filed with the SEC by Wellington Management Group LLP on February 11, 2016. According to the Schedule 13G, Wellington Management Group LLP has shared voting power over 4,888,214 shares of our common stock and shared dispositive power over 5,509,936 shares of our common stock. The shares of our common stock that are beneficially owned by Wellington Management Group LLP are owned of record by clients of one or more investment advisers directly or indirectly controlled by Wellington Management Group LLP. These clients have the right to receive, or the power to direct the receipt of, dividends from, or the proceeds from the sale of, such shares. No such client is known to have such right or power with respect to more than five percent of the shares of our common stock.

(d) Based on the Schedule 13G filed with the SEC by Vanguard Group Inc. on February 11, 2016. According to the Schedule 13G, Vanguard Group Inc. has sole voting power over 122,966 shares of our common stock, shared voting power over 4,600 shares of our common stock, sole dispositive power over 5,288,274 shares of our common stock and shared dispositive power over 123,296 shares of our common stock. The Schedule 13G reports that Vanguard Fiduciary Trust Company, a wholly owned subsidiary of Vanguard Group Inc., is the beneficial owner of 118,696 shares of our common stock as a result of its serving as investment manager of collective trust accounts and that Vanguard Investments Australia, Ltd., a wholly owned subsidiary of Vanguard Group Inc., is the beneficial owner of 8,900 shares of our common stock as a result of its serving as investment manager of Australian investment offerings.

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Security Ownership of Management

The following table sets forth information regarding the number of shares of our common stock beneficially owned on April 21, 2016, by:

- each of our directors;
- each of our named executive officers; and
- all of our directors and executive officers presently serving, as a group.

Except as otherwise set forth below, the address of each of the persons listed below is c/o Hilltop Holdings Inc., 200 Crescent Court, Suite 1330, Dallas, Texas 75201. Except as otherwise indicated in the footnotes to this table, the persons named in the table have specified that they have sole voting and investment power with respect to all shares of stock shown as beneficially owned by them, subject to any applicable community property law.

Name of Beneficial Owner	Common Stock Amount and Nature of Beneficial Ownership		Percent of Class (a)
Charlotte Jones Anderson	7,093		*
Rhodes Bobbitt	126,059	(b)	*
Tracy A. Bolt	12,945		*
W. Joris Brinkerhoff	25,228		*
J. Taylor Crandall	—	(c)	*
Charles R. Cummings	37,476		*
Hill A. Feinberg	1,236,752	(d)	1.3%
Gerald J. Ford	15,560,490	(e)	15.8%
200 Crescent Court, Suite 1350			
Dallas, Texas 75201			
Jeremy B. Ford	617,438	(f)	*
J. Markham Green	119,152		*
William T. Hill, Jr.	54,350	(g)	*
James R. Huffines	369,730	(h)	*
Lee Lewis	656,199	(i)	*
Andrew J. Littlefair	10,546		*
W. Robert Nichols, III	41,000	(j)	*
Darren Parmenter	5,361	(k)	*
C. Clifton Robinson	1,235,024		1.3%
Kenneth D. Russell	—		*
Todd L. Salmans	14,662	(l)	*
A. Haag Sherman	14,422		*
Robert C. Taylor, Jr.	32,585		*
Carl B. Webb	108,490		*

Alan B. White	1,686,947	(m)	1.7%
All Directors and Executive Officers, as a group (26 persons)	22,276,414	(n)	22.6%

* Represents less than 1% of the outstanding shares of such class.

(a) Based on 98,498,077 shares of common stock outstanding on April 21, 2016. Shares issuable under instruments to purchase our common stock that are exercisable within 60 days of April 21, 2016 are treated as if outstanding for computing the percentage ownership of the person holding these instruments, but are not treated as outstanding for purposes of computing the percentage ownership of any other person.
(b) Includes 62,100 shares of common stock held in an IRA account for the benefit of Mr. Bobbitt.
(c) Excludes 1,488 shares held by Oak Hill Capital Management LLC, 69,014 shares held by Oak Hill Capital Management Partners III, L.P. and 2,101,418 shares held by Oak Hill Capital Partners III, L.P.
(d) Includes 25,776 shares of common stock held directly by Mr. Feinberg's wife. Also includes 776 shares of common stock held by the Max McDermott Trust for the benefit of Mr. Feinberg's stepson. Mr. Feinberg's wife is the trustee of the trust. Excludes 40,579 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016.

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(e) The shares of common stock beneficially owned by Mr. Gerald J. Ford include 7,950 shares that are owned by Turtle Creek Revocable Trust, a revocable trust for the benefit of the members of Mr. Gerald J. Ford's family, and indirectly by Mr. Gerald J. Ford as settlor of the trust. Mr. Gerald J. Ford disclaims beneficial ownership of the shares held by the trust except to the extent of his pecuniary interest therein. Also includes 15,544,674 shares owned by Diamond A Financial, LP. Mr. Gerald J. Ford is the sole general partner of Diamond A Financial, LP. Mr. Gerald J. Ford has sole voting and dispositive power of these shares. Excludes 60,000 RSUs that will not vest within 60 days of April 21, 2016.

(f) Jeremy B. Ford is a beneficiary of a trust that owns a 49% limited partnership interest in Diamond A Financial, LP (see footnote (e)). Excludes 105,341 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016 and 15,544,674 shares of common stock held by Diamond A Financial, LP.

(g) Includes 7,300 shares of common stock held in a SEP IRA account for the benefit of Mr. Hill and 15,750 shares of common stock held by the William T. Hill P.C. retirement account for the benefit of Mr. Hill.

(h) Includes 47,000 shares of common stock held by the James Huffines 1994 Trust for the benefit of Mr. Huffines and 12,028 shares of common stock held in a self-directed individual retirement account. Excludes 65,744 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016.

(i) Includes 603,417 shares of common stock held by Lee Lewis Construction. Mr. Lewis is the sole owner of Lee Lewis Construction and may be deemed to have voting and/or investment power with respect to the shares owned by Lee Lewis Construction.

(j) Includes 11,000 shares of common stock held in an IRA account for the benefit of Mr. Nichols.

(k) Excludes 27,394 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016.

(l) Excludes 54,787 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016.

(m) Includes (a) 9,785 shares of common stock held directly by Mr. White's wife, (b) 453 shares of common stock held in a self-directed individual retirement account of Mr. White's wife, (c) 23,806 shares of common stock held by Double E Investments ("Double E"), (d) 12,883 shares of common stock held by EAW White Family Partnership, Ltd. ("EAW"), (e) 8,045 shares of common stock held by Maedgen, White and Maedgen ("MW&M"), (f) 1,366,458 shares of common stock held by Maedgen & White, Ltd., and (g) 95,844 shares of common stock held in a self-directed individual retirement account of Mr. White. As the manager of Double E, the managing partner of MW&M and the sole member of the general partner of EAW, Mr. White has exclusive authority to vote and/or dispose of the securities held by Double E, MW&M and EAW, respectively, and may, therefore, be deemed to have sole voting and dispositive power over the shares of common stock held by Double E, MW&M and EAW. Mr. White is the sole general partner of Maedgen & White, Ltd. and may be deemed to beneficially own the shares held by Maedgen & White, Ltd. As the sole general partner of Maedgen & White, Ltd., Mr. White has the power to vote the shares held by Maedgen & White, Ltd. The Agreement of Limited Partnership of Maedgen & White, Ltd. requires the approval of 80% of the limited partnership interests in Maedgen & White, Ltd. before its general partner may dispose of the shares held by Maedgen & White, Ltd. Mr. White, directly and indirectly, controls approximately 77% of the limited partnership interests of Maedgen & White, Ltd. and therefore may be deemed to share dispositive power over the shares held by Maedgen & White, Ltd. Excludes 109,573 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016.

(n) Represents 26 persons and includes 100,000 shares of common stock exercisable pursuant to stock options that are vested. Excludes 597,254 shares of common stock deliverable upon the vesting of RSUs that will not vest within 60 days of April 21, 2016.

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MANAGEMENT

Executive Officers

General

We have identified the following officers as “executive officers,” consistent with the definition of that term as used by the SEC:

Name	Age	Position	Officer Since
Hill A. Feinberg	69	Chairman and Chief Executive Officer of Hilltop Securities	2012
Jeremy B. Ford	41	President, Chief Executive Officer and Director	2010
James R. Huffines	65	President and Chief Operating Officer of PlainsCapital	2012
John A. Martin	68	Executive Vice President, Chief Financial Officer of PlainsCapital	2012
Darren E. Parmenter	53	Executive Vice President, Principal Financial Officer	2007
Corey G. Prestidge	42	Executive Vice President, General Counsel and Secretary	2008
Todd L. Salmans	67	Chief Executive Officer of PrimeLending	2012
Jerry L. Schaffner	58	President and Chief Executive Officer of PlainsCapital Bank	2012
Alan B. White	67	Chairman and Chief Executive Officer of PlainsCapital	2012

Business Experience of Executive Officers

Information concerning the business experience of Messrs. Hill A. Feinberg, Jeremy B. Ford, James R. Huffines and Alan B. White is set forth above under “Proposal One — Election of Directors — Nominees for Election as Directors” beginning on page 6.

John A. Martin. Mr. Martin has served as the Executive Vice President and Chief Financial Officer of PlainsCapital since November 2010 and has continued in that position since our acquisition of PlainsCapital in November 2012. Mr. Martin also serves on the board of directors of the Bank and various other subsidiaries of PlainsCapital. Prior to joining PlainsCapital, Mr. Martin most recently served as executive vice president and chief financial officer of Family Bancorp, Inc. and its subsidiary, San Antonio National Bank, from April 2010 until October 2010. Before joining Family Bancorp, from 2009 to 2010, Mr. Martin served as a consultant to community banks, providing strategic planning services. Beginning in 2005, Mr. Martin served as chief financial officer of Texas Regional Bancshares, Inc. and later served as director of financial planning and analysis for BBVA Compass after its

acquisition of Texas Regional Bancshares in 2006.

Darren E. Parmenter. Mr. Parmenter has served as Executive Vice President and Principal Financial Officer of Hilltop since February 2014 and previously served as Senior Vice President of Finance of Hilltop from June 2007 to February 2014. From January 2000 to June 2007, Mr. Parmenter was with Hilltop's predecessor, Affordable Residential Communities Inc., and served as the Controller of Operations from April 2002 to June 2007. Prior to 2000, Mr. Parmenter was employed by Albertsons Inc. as an Assistant Controller.

Corey G. Prestidge. Mr. Prestidge has served as an Executive Vice President of Hilltop since February 2014 and General Counsel and Secretary of Hilltop since January 2008. From November 2005 to January 2008, Mr. Prestidge was the Assistant General Counsel of Mark Cuban Companies. Prior to that, Mr. Prestidge was an associate in the corporate and securities practice group at Jenkens & Gilchrist, a Professional Corporation, which is a former national law firm. Mr. Prestidge is the son-in-law of our Chairman of the Board, Gerald J. Ford, and the brother-in-law of our President and Chief Executive Officer, Jeremy B. Ford.

Todd L. Salmans. Mr. Salmans has served as Chief Executive Officer of PrimeLending since January 2011 and has continued in that position since our acquisition of PlainsCapital in November 2012. He also previously held the office of President of PrimeLending until August 2013. As Chief Executive Officer, Mr. Salmans is responsible for the strategic direction and day-to-day management of PrimeLending, including financial performance, compliance, business development, board and strategic partner communications and team development. He also serves as a member of PrimeLending's Board of Directors. Mr. Salmans joined PrimeLending in 2006 as Executive Vice President and Chief

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Operating Officer, with responsibility over daily operations, loan processing and sales. He was promoted to President in April 2007. Mr. Salmans has over 30 year of experience in the mortgage banking industry. Prior to joining PrimeLending, he served as regional executive vice president of CTX/Centex, regional senior vice president of Chase Manhattan/Chase Home Mortgage Corp., and regional senior vice president of First Union National Bank/First Union Mortgage Corp. Mr. Salmans is currently a board member of the Texas Mortgage Bankers Association.

Jerry L. Schaffner. Mr. Schaffner has served as the President and Chief Executive Officer of the Bank since November 2010 and has continued in that position since our acquisition of PlainsCapital in November 2012. He currently serves as a director of the Bank and various other subsidiaries, and previously served as a director of PlainsCapital from 1993 until March 2009. Mr. Schaffner joined PlainsCapital in 1988 as part of its original management group.

Terms of Office and Relationships

Our executive officers are elected annually or, as necessary, to fill vacancies or newly created offices by our Board of Directors. Each executive officer holds office until his successor is duly elected and qualified or, if earlier, until his death, resignation or removal. Any officer or agent elected or appointed by our Board of Directors may be removed by our Board of Directors whenever, in its judgment, our best interests will be served, but any removal will be without prejudice to the contractual rights, if any, of the person so removed.

Except as disclosed under “Proposal One — Election of Directors — Nominees for Election as Directors” commencing on page 6 and under “Management — Executive Officers — Business Experience of Executive Officers” on page 26, (a) there are no familial relationships among any of our current directors or executive officers and (b) none of our director nominees hold directorships in any company with a class of securities registered pursuant to Section 12 of the Exchange Act or pursuant to Section 15(d) of the Exchange Act or any company registered as an investment company under the Investment Company Act of 1940.

Except as set forth in this Proxy Statement, there are no arrangements or understandings between any nominee for election as a director or officer and any other person pursuant to which that director was nominated or that officer was selected.

Compensation Discussion and Analysis

This Compensation Discussion & Analysis section reviews the compensation program for our five current named executive officers (“NEOs”), which include our principal executive officer, principal financial officer and our three

other most highly-compensated executive officers for the year ended December 31, 2015.

Our 2015 NEOs were:

Named Executive Officer	Title/Role
Jeremy B. Ford	President and Chief Executive Officer
Darren E. Parmenter	Executive Vice President, Principal Financial Officer
Alan B. White	Chief Executive Officer of PlainsCapital
James R. Huffines	President and Chief Operating Officer of PlainsCapital
Todd L. Salmans	Chief Executive Officer of PrimeLending

2015 Business and Financial Highlights

2015 represented another strong year for the Company. In 2015, we continued to grow and expand into a diversified financial holding company through the completion of our acquisition of SWS in January 2015. In addition, we had the following accomplishments during 2015:

· We generated $209 million in income applicable to common stockholders, or $2.09 per diluted share, during 2015. Return on average equity was 12.32% and return on average assets was 1.70% for 2015.

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- Asset quality improved and remained strong compared to peers with non-performing assets as a percentage of total assets of 0.21% as of December 31, 2015, excluding covered loans and covered other real estate owned.
- Hilltop capital ratios remained strong with a Tier 1 Leverage Ratio at 12.65% and a Total Risk Based Capital Ratio of 18.89% at December 31, 2015.
- Integrated Southwest Securities, FSB into PlainsCapital Bank by May 2015 and made significant progress on the integration of our broker-dealer subsidiaries allowing us to complete the reorganization of the broker-dealers into one unit in January 2016.
- Completed a senior notes offering on favorable terms that provided us with the proceeds to redeem all of our Small Business Lending Fund, or SBLF, preferred stock. The SBLF preferred stock dividend rate would have increased in 2016.

All of this contributed to an increase in our book value per share from $14.93 at December 31, 2014 to $17.56 at December 31, 2015. Additional detail regarding our results and achievements can be found in our Annual Report on Form 10-K for the year ended December 31, 2015.

Our 2015 Executive Compensation Program

Overview

The Compensation Committee, or, in this Compensation Discussion and Analysis, the Committee, has the responsibility to establish, implement and monitor adherence with our compensation philosophy. The Committee ensures that the total compensation paid to executive officers is fair, reasonable, competitive, performance-based and aligned with stockholder interests. The Committee administers the Company’s executive compensation program in light of our unique structure and acquisition history. As a holding company that conducts its operations through its subsidiaries, we are focused on providing entrepreneurial-based compensation to the chief executives of each of our business units.

Philosophy and Objectives of Our Executive Compensation Program

Our compensation program continues to focus on performance-based pay that reflects our achievements on an annual basis and our ability to deliver long-term value to our stockholders. The Compensation Committee regularly reviews the Company’s compensation programs to ensure they are consistent with safe and sound business practices, regulatory requirements, emerging industry trends and stockholder interests.

With this in mind, the following principles help guide our decisions regarding compensation of our NEOs:

- Compensation opportunities should be competitive with market practices. We are committed to providing competitive total annual compensation opportunities in order to attract and retain executives with the experience and skills necessary to lead our Company and motivate them to deliver strong performance to our stockholders.
- A significant portion of compensation should be performance-based. Our executive compensation program emphasizes pay-for-performance. Both our annual and long-term incentives are earned based on a combination of corporate, business unit and individual performance. Our annual incentive compensation also can be reduced based upon improper risk taking and non-compliance with applicable laws and regulations.
- Management's interests should be aligned with those of our stockholders. Our long-term incentive compensation is delivered in the form of RSUs to support our goals for alignment, ownership and retention. Half of the RSUs awarded vest upon achievement of predefined performance goals. The value of previous awards ultimately depends upon our relative total stockholder return and our cumulative earnings per share, or EPS, over a three-year period. Commencing in 2016, the percentage of these awards that vest is based first on cumulative earnings per share over a three-year period and then multiplied by a modifier based on our relative total stockholder return during the same period.
- Compensation should be perceived as fair. We strive to create a compensation program that will be perceived as fair and equitable, both internally and externally.

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- Our compensation program should be balanced and mitigate risk taking. We have a balanced approach to total compensation that includes a mix of base/fixed pay, a proportion of cash and equity and a proportion of short- and long-term incentive compensation that we believe effectively aligns our pay with performance while discouraging inappropriate risk taking.

For the fiscal year 2015, our target pay mix for the Chief Executive Officer, or CEO, of Hilltop and our remaining NEOs was the following:

Governance highlights

The Compensation Committee continued to maintain the following compensation best practices:

- Robust stock ownership guidelines for executive officers and directors
- Clawback policy for incentive compensation
- Anti-hedging and pledging policy
- Limited perquisites
- No excise tax gross-ups in new employment agreements
- One year holding requirement on all vested equity awards
- Annual compensation risk assessment

How We Determine and Assess Executive Compensation Generally

Background

We completed the acquisition of PlainsCapital Corporation on November 30, 2012, and the compensation of our NEOs who were employed by PlainsCapital Corporation is, therefore, in part based upon the compensation they were paid by PlainsCapital Corporation prior to the acquisition. Three of our NEOs, Messrs. White, Huffines and Salmans, were employed by PlainsCapital Corporation or its subsidiaries prior to the acquisition. In connection with the acquisition of PlainsCapital Corporation, we entered into a retention agreement with Mr. White to ensure continuity following the closing that was negotiated based upon the pre-existing rights in his employment agreement with PlainsCapital Corporation. All other existing employment arrangements at PlainsCapital Corporation were amended to terminate on November 30, 2014. Following the expiration of the employment agreements with Messrs. Huffines and Salmans, we entered into new employment agreements with them that are consistent with our current compensation philosophy. For a more detailed discussion of these employment agreements and Mr. White's retention agreement, see

“Executive Compensation — Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table — Employment Contracts and Incentive Plans — Employment Contracts.”

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Role of the Compensation Committee

The Committee is responsible for reviewing and approving all aspects of the compensation programs for our NEOs and making all decisions regarding specific compensation to be paid or awarded to them. The Committee is responsible for, among its other duties, the following:

- Review and approval of corporate incentive goals and objectives relevant to compensation;
- Evaluation of individual performance results in light of these goals and objectives;
- Evaluation of the competitiveness of the total compensation package; and
- Approval of any changes to the total compensation package, including, but not limited to, base salary, annual and long-term incentive award opportunities and payouts and retention programs.

The Committee is responsible for determining all aspects of compensation of the Chief Executive Officers of Hilltop and PlainsCapital, as well as assessing their individual performance.

In setting the compensation of our NEOs, the Committee, in its discretion, considers (i) the transferability of managerial skills, (ii) the relevance of each NEO's experience to other potential employees, and (iii) the readiness of the NEO to assume a different or more significant role, either within our organization or with another organization. When the Committee makes pay-related decisions, the Committee considers our acquisition and growth strategy, our desire to attract, retain and motivate talent, and the importance of compensation in supporting the achievement of our strategic objectives.

Information about the Committee and its composition, responsibilities and operations can be found under the "Board Committees" section.

Role of the Chief Executive Officers in Compensation Decisions

The Chief Executive Officers of Hilltop and PlainsCapital recommend to the Committee any compensation changes affecting the other NEOs. The Chief Executive Officers provide input and recommendations to the Committee with regards to compensation decisions for their direct reports. These recommendations are made within the framework of the compensation programs approved by the Committee and based on market data provided by the Committee's independent consultant. The input includes base salary changes, annual incentive and long-term incentive opportunities and payouts, specific individual performance objectives, and individual performance assessments. The Chief Executive Officers make their recommendations based on their assessment of the individual officer's performance, performance of the officer's respective business or function and employee retention considerations. The Committee reviews and considers the Chief Executive Officers' recommendations when determining any

compensation changes affecting our officers or executives. Each Chief Executive Officer does not play any role with respect to any matter impacting his own compensation.

Role of Stockholder Say-on-Pay Votes

The Company provides its stockholders with the opportunity to cast an annual advisory vote on executive compensation. At the Company's annual meeting of stockholders held in June 2015, over 98% of the votes cast (excluding abstentions and broker non-votes) on the say-on-pay proposal at that meeting were voted in favor of the proposal. Given this significant level of support from the Company's stockholders, the Committee and the Board of Directors believe that the Company is taking a measured, informed and responsible approach to executive compensation that incorporates all of the Company's objectives and policies set forth above, including, but not limited to, a pay for performance culture that retains executives who perform strongly. Accordingly, the Committee will continue to consider the outcome of the Company's say-on-pay votes when making future compensation decisions for the NEOs.

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Role of Compensation Consultant

Pursuant to its charter, the Committee is authorized to retain and terminate any consultant, as well as to approve the consultant's fees and other terms of the engagement. The Committee also has the authority to obtain advice and assistance from internal or external legal, accounting or other advisors. In 2015, the Committee continued its engagement of Meridian Compensation Partners, LLC ("Meridian") as its independent compensation consultant.

Meridian provides research, data analyses, survey information and design expertise in developing compensation programs for executives and incentive programs for eligible employees. In addition, Meridian keeps the Committee apprised of regulatory developments and market trends related to executive compensation practices. Meridian does not determine or recommend the exact amount or form of executive compensation for any of the NEOs. A representative of Meridian generally attends meetings of the Committee, is available to participate in executive sessions and communicates directly with the Committee and the chairman of the Committee.

Pursuant to the Committee's charter, if the Committee elects to use a compensation consultant, the Committee must assess the consultant's independence, taking into account the following factors:

- The provision of other services to the Company by the consultant;
- The amount of fees the consultant received from the Company;
- the policies and procedures the consultant has in place to prevent conflicts of interest;
- any business or personal relationships between the consulting firm and the members of the Committee;
- any ownership of Company stock by the individuals at the firm performing consulting services for the Committee; and
- any business or personal relationship of the firm with an executive officer of the Company.

Meridian has provided the Committee with appropriate assurances and confirmation of its independent status pursuant to the charter and other factors. The Committee believes that Meridian has been independent throughout its service for the Committee and there is no conflict of interest between Meridian and the Committee.

Other Factors

The Committee makes executive compensation decisions following a review and discussion of both the financial and operational performance of our businesses and the annual performance reviews of the NEOs and other members of the management team.

Benchmarking Compensation

The Committee regularly assesses the components of the executive compensation program with advice from its independent compensation consultant. In November 2014, Meridian provided an analysis of base salary, annual incentive and long-term incentive practices of comparable companies in the financial industry. Meridian considered individual compensation elements as well as the total compensation package.

In performing this analysis, Meridian used a peer group of financial institutions. In order to reflect the Company's continued growth, and in anticipation of the merger with SWS, the Committee approved a new peer group in July 2014. The peer group included institutions of generally similar asset size and, to the extent possible, organizations with significant other operating segments. The peer group is comprised of 22 banks with assets between $6.3 billion and $26.5 billion as of June 30, 2014. Hilltop's post-merger asset size of $12.6 billion was positioned slightly below the median of the new peer group.

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The peer group used in the report presented for consideration in the determination of 2015 pay consisted of the following financial institutions:

Associated Banc-Corp	Cullen/Frost Bankers, Inc.	First Citizens BancShares, Inc.
First Horizon National Corporation	First Midwest Bancorp, Inc.	FirstMerit Corporation
Hancock Holding Company	IBERIABANK Corporation	International Bancshares Corporation
MB Financial, Inc.	Old National Bancorp	Prosperity Bancshares, Inc.
South State Corporation	TCF Financial Corporation	Texas Capital Bancshares, Inc.
Trustmark Corporation	UMB Financial Corporation	Umpqua Holdings Corporation
Union Bankshares Corporation	United Bankshares, Inc.	WesBanco, Inc.
Wintrust Financial Corporation		

In addition to the peer group, Meridian included data from industry-specific compensation surveys. The information from these competitive data sources and the peer group were used to make 2015 compensation decisions.

Elements of our Executive Compensation Program

The basic elements of our executive compensation program are summarized below. Our compensation policies and programs are considered by the Committee in a total rewards framework, which considers both “pay” — base salary, annual incentive awards and long-term incentive awards — and “benefits” — perquisites and other benefits and other compensation. Our executive compensation program consists primarily of the following components:

Compensation Component	Purpose
Base Salary	Fixed component of pay intended to compensate the individual fairly for the responsibility level of the position held.
Annual Incentive Awards	Variable component of pay intended to motivate and reward the individual's contribution to achieving our short-term/annual objectives.
Long-term Incentive Awards	Variable component of pay intended to retain, motivate and reward the individual's contribution to achieving our long-term objectives and creating stockholder value.
Perquisites and Other Benefits	Fixed component of pay intended to provide an economic benefit to us in attracting and retaining executive talent.

Base Salary

We provide base salaries for each NEO commensurate with the services each provides to us. We believe a portion of total direct compensation should be provided in a form that is fixed and liquid. In reviewing base salaries, the Committee evaluated the salaries of other executive officers of the Company and its peers and any increased level of responsibility, among other items. As a result of that analysis, the Committee determined to increase the annual salaries of Messrs. Ford and Parmenter effective April 1, 2015. With respect to the other NEOs of the Company, the Committee determined to maintain the current salary for 2015, as they were found to be competitive with the Company's peers. The following are the base salaries for our NEOs in 2014 and 2015:

	Base Salary		
Name	2014	2015	$ Change
Jeremy B. Ford	$ 550,000	$ 700,000	$ 150,000
Darren E. Parmenter	$ 330,000	$ 335,000	$ 5,000
Alan B. White	$ 1,350,000	$ 1,350,000(a)	$ —
James R. Huffines	$ 690,000	$ 690,000	$ —
Todd L. Salmans	$ 750,000	$ 750,000	$ —

(a) Mr. White's base salary is set forth in his retention agreement, which became effective upon the closing of the acquisition of PlainsCapital Corporation.

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In February 2016, the Committee assessed base salaries of the NEOs and decided to maintain the current salary of the Company's NEOs.

Annual Incentive Awards

Our NEOs and other employees are eligible to participate in the Annual Incentive Plan and receive annual cash incentive awards based upon our financial performance and other factors, including individual performance. The Committee believes that this element of compensation is important to focus management efforts on, and provide rewards for, annual financial and strategic results that are aligned with creating value for our stockholders.

Target Annual Incentive Opportunities

Target incentive awards are defined at the start of the year in consideration of market data provided by the Committee's consultant, each executive's total compensation package and the entity's budgetary considerations. In consideration of these factors, the Committee slightly increased 2015 targets for Messrs. Ford, Huffines and Parmenter but maintained target incentive opportunities for the other NEOs.

	Annual Incentive Value				
	Threshold	Target	% of Annual		Maximum
Name	($)	($)	Base Salary		($)
Jeremy B. Ford	108,000	600,000	86	%	750,000
Darren E. Parmenter	28,200	235,000	70	%	293,750
Alan B. White (a)	1,350,000	1,350,000	100	%	1,350,000
James R. Huffines	99,900	555,000	80	%	693,750
Todd L. Salmans	90,000	750,000	100	%	937,500

(a) Mr. White's annual incentive compensation is determined pursuant to his retention agreement for the achievement of specified performance criteria.

Performance Measures

Each NEO had pre-defined performance objectives based upon measurable performance of both the individual and our Company, other than Mr. White, whose pre-defined performance objectives are based solely upon PlainsCapital's performance. Our 2015 goals were intended to be realistic and reasonable but challenging in order to drive

performance. The Committee and management believe that by using these metrics we are encouraging profitable top line growth and value for stockholders without creating excessive risk. For 2015, the applicable performance goals included:

- Consolidated net income for Hilltop for NEOs employed by Hilltop;
- Consolidated net income of PlainsCapital for employees of PlainsCapital and its subsidiaries;
- Net income results of lines of business for business heads; and
- Pre-determined strategic initiatives and individual objectives.

The weights of these factors are summarized in the following table:

Name	Hilltop Performance	PlainsCapital Performance	Business Unit Performance	Strategic Initiatives
Jeremy B. Ford	70 %	—	—	30 %
Darren E. Parmenter	50 %	—	20 %	30 %
Alan B. White (a)	—	100 %	—	—
James R. Huffines	—	70 %	—	30 %
Todd L. Salmans	—	20 %	50 %	30 %

(a) Determined pursuant to Mr. White's retention agreement for the achievement of earnings threshold.

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The individual strategic objectives for the NEOs are developed through an iterative process between the Committee and management. Management develops an initial set of recommendations based upon the business needs. The Committee reviews the proposed goals and revises/amends them at their discretion, ensuring that goals are aligned with the Board of Director's strategic focus. The following goals, among others, were established for the NEOs in 2015:

- Mr. Jeremy B. Ford's strategic initiatives included: execute the Company's 2015 strategic plan, continue to identify strategic acquisition opportunities that complement the Company's business mix, continue to integrate recent acquisitions and increase net earnings.
  - Mr. Parmenter's strategic initiatives included: facilitate acquisition activity including effective integration of accounting departments and consolidation of Hilltop's financials, and provide effective leadership of his responsible business units.
- Mr. Huffines strategic initiatives included: grow core business and achieve quantitative cost savings through integration of mergers and acquisitions.
- Mr. Salmans's strategic initiatives included: execute three-year business strategy for PrimeLending, continue succession planning and talent development for key positions and achieve cost savings from implementation of strategic plan.

Performance Results and Payouts

The Committee, in its sole discretion, determines the final amount of each participant's award based on attainment of the applicable performance goals and assessments of individual and strategic performance. Additionally, a forfeiture of up to 15% of any available Annual Incentive Plan award can occur in the event that any improper risk management or non-compliance with applicable laws or regulations is identified.

Each element of the annual cash incentive award is independent of the other. Accordingly, the executive officer may achieve certain performance goals, while at the same time failing to achieve others. In that case, the executive officer will be entitled to receive the award for the performance goal achieved, but not an award for a performance goal for which threshold performance is not achieved. Potential awards ranged from 50% for threshold performance to a maximum of 150% for stretch performance.

At the end of the fiscal year, the Committee determined a payout based on net income performance. 2015 performance goals and actual net income performance were as follows (dollars in millions):

2015 Performance Goal	Threshold ($)	Target ($)	Stretch ($)	Actual ($)	Achievement	
Hilltop Adjusted Net Income (a)	65.1	108.4	162.6	145.2	134	%
PlainsCapital Net Income	57.9	96.5	144.7	140.5	146	%

PrimeLending Net Income	11.5	19.2	28.8	32.4	169	%

(a) Hilltop net income was adjusted to exclude bargain purchase gain and acquisition and integration costs, which were not included in the 2015 strategic plan.

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Based upon evaluation of their respective individual performance in 2015, the Committee awarded each of the NEOs a score of 100% for strategic initiatives. Based on the above financial and individual performance measures and the Committee's discretion, the 2015 annual cash incentive payments were awarded as follows relative to the 2015 target value:

Name	2015 Annual Incentive Payment ($)	% of 2015 Target Annual Incentive	
Jeremy B. Ford	740,000	123	%
Darren E. Parmenter	290,000	123	%
Alan B. White (a)	1,350,000	100	%
James R. Huffines	555,000	100	%
Todd L. Salmans	1,000,000	133	%

(a) Determined pursuant to Mr. White's retention agreement for the achievement of earnings threshold.

See "Executive Compensation — Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table — Annual Incentive Plan" for more information on possible future payments to the NEOs.

Long-Term Incentive Awards

As described above, we believe that a portion of each NEO's compensation should be tied to the performance of our stock price, aligning the officer's interest with that of our stockholders. In this regard, the Committee determined that the award vehicle mix should be:

Award Vehicle Mix	% of Award
Time-Based Restricted Stock Units	50%
Performance-Based Restricted Stock Units	50%

Time-based RSUs cliff vest on the third anniversary of grant date. Performance-based RSUs are earned and cliff vest after the three-year performance period from January 1, 2015 through December 31, 2017. Performance awards are earned based on Hilltop's three-year cumulative EPS and based on relative total stockholder return, or TSR, relative to

the KBW Regional Banking Index.

Commencing in 2016, a revision was made to the method of calculating performance for awarding performance-based RSUs. Under the revised form of award, the percentage of performance-based RSUs that vest following a performance period is based on Hilltop's three-year cumulative EPS multiplied by a modifier that is determined based on Hilltop's TSR relative to the KBW Regional Banking Index. The new method of measuring performance puts more weight on EPS and uses TSR as a modifier, instead of weighting each measure equally. The EPS component of performance calculation ranges from 50% at threshold to 150% at the max, and the TSR modifier ranges from 80% at threshold to 120% at max. The total number of shares earned from the performance awards can range from 40% to 180% of the target number of RSUs granted.

All shares of common stock delivered pursuant to the RSUs are subject to a one-year holding period requirement after vest. Further discussion of the 2012 Equity Incentive Plan pursuant to which such RSUs were awarded is found under "Executive Compensation — Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table" below.

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In 2015, long-term incentive awards were made in consideration of each executive's role, competitive market practice, and performance. Grants were made in the form of RSUs on February 24, 2015, to the following NEOs as set forth below:

Name	Time-Based RSUs Awarded	Performance-Based RSUs Awarded (at Target)	Total RSUs Awarded
Jeremy B. Ford	18,004	18,004	36,008
Darren E. Parmenter	4,501	4,501	9,002
Alan B. White	18,004	18,004	36,008
James R. Huffines	10,803	10,802	21,605
Todd L. Salmans	9,002	9,002	18,004

On February 23, 2016, the Committee continued the same mix of long-term incentive awards and approved a grant of RSUs to the NEOs as set forth below:

Name	Time-Based RSUs Awarded	Performance-Based RSUs Awarded (at Target)	Total RSUs Awarded
Jeremy B. Ford	21,971	21,971	43,942
Darren E. Parmenter	5,493	5,493	10,986
Alan B. White	21,971	21,971	43,942
James R. Huffines	13,183	13,182	26,365
Todd L. Salmans	10,986	10,985	21,971

Mr. Jeremy B. Ford recently exercised an award outstanding under the 2003 Equity Incentive Plan. However, with the adoption of the 2012 Equity Incentive Plan, all equity-based awards, including those made to the NEOs, have since been made pursuant to the 2012 Equity Incentive Plan. All equity-based awards made to the NEOs are approved by the Committee and not pursuant to delegated authority.

Perquisites and Other Benefits

We provide a limited number of perquisites and other benefits to our NEOs at Hilltop. The only perquisite currently offered to Messrs. Jeremy B. Ford and Parmenter, the NEOs employed directly by Hilltop is $150 per month to be

applied to a gym membership to promote wellness. In addition, Mr. Jeremy B. Ford is provided access to company aircraft. With respect to NEOs employed by PlainsCapital and its subsidiaries, those entities provide them with a monthly car allowance and reimbursement for country club membership dues. In addition, Mr. White is provided access to company aircraft and bank-owned life insurance. Otherwise, generally, our NEOs receive only medical benefits, life insurance and long-term disability coverage, as well as supplemental contributions to the Company's 401(k) program, on the same terms and conditions as available to all employees of that entity.

Severance and Other Post-Termination Compensation

On December 4, 2014, we entered into new employment agreements with Messrs. Huffines and Salmans. A description of these new employment agreements and the post-contractual benefits provided thereunder is discussed in further detail under "Executive Compensation — Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table — Employment Contracts and Incentive Plans — Employment Contracts" and "Potential Payments Upon Termination or Change-in-Control" below.

For NEOs employed directly by Hilltop, other than change in control provisions in our 2012 Equity Incentive Plan, we do not currently maintain any severance or change in control programs. However, we have historically paid severance, the amount of which is generally determined both by length of tenure and level of compensation, when termination occurs other than for cause and pursuant to which certain benefits may be provided to the NEOs. Absent the negotiation of specific agreements with the NEOs, severance benefits would be provided on the same basis as provided to other employees of the Company.

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In connection with our acquisition of PlainsCapital in 2012, we entered into a retention agreement with Mr. White which was approved by shareholders of PlainsCapital Corporation in connection with our acquisition of PlainsCapital Corporation. The summary of the severance terms for this retention agreement is set forth below:

Legacy Retention Agreement

Pursuant to Mr. White's retention agreement:

(1) we agreed to contribute an amount of cash equal to $6,430,890 as deferred compensation to Mr. White in satisfaction of Mr. White's rights under Section 6 (Termination Upon Change in Control) of his previous employment agreement with PlainsCapital, which such amount accrues interst at the prevailing money market rate and is payable to Mr. White on the 55th day following termination of his employment; and
(2) upon a termination of his employment by us other than for cause or death or disability, or after non-renewal, cash severance of (i) the sum of Mr. White's annual base salary and the average of the annual bonus amounts paid to him for the three most recently completed fiscal years ending immediately prior to the date of termination, multiplied by (ii) the greater of (A) two, and (B) the number of full and partial years from the date of termination through the end of the applicable employment period under the retention agreement. Such severance is payable over the "severance period," which is the greater of two years from the date of termination and the number of full and partial years from the date of termination through the end of the applicable employment period under the retention agreement.

The foregoing cash amounts in subparagraph (1) represent "modified single trigger" benefits, payable assuming the termination of employment for any reason, and the foregoing cash amounts in subparagraph (2) represent "double trigger" benefits, payable assuming a qualifying termination of employment. With respect to the amounts described in subparagraph (1) that are paid in full satisfaction of Section 6 of Mr. White's previous employment agreement with PlainsCapital, such amounts are payable upon any termination of employment at any time, subject to any delay required by Section 409A of the Internal Revenue Code (the "Code") and the execution of a release of claims. The cash severance amounts described in subparagraph (2) are payable upon a termination of employment other than for cause, death or disability or upon a termination due to non-renewal by Hilltop, subject to any delay required by Section 409A of the Code and the execution of a release of claims.

Huffines and Salmans Employment Agreements

Pursuant to our employment agreements with Messrs. Huffines and Salmans, upon termination of employment by us other than for cause, the applicable executive is entitled to a lump-sum cash payment equal to the sum of (i) his annual base salary rate immediately prior to the effective date of such termination, and (ii) an amount equal to the annual incentive cash bonus paid to him in respect of the calendar year immediately preceding the year of the termination. If his employment is terminated without "cause" within the twelve months immediately following, or the six months

immediately preceding, a “change in control,” he will be entitled to receive a lump-sum cash payment equal to two times the sum of (A) his annual base salary rate immediately prior to the effective date of such termination and (B) an amount equal to the annual incentive cash bonus paid to him in respect of the calendar year immediately preceding the year of the termination. The immediately foregoing cash amount represents a “double trigger” benefit. Finally, if any payment made as a result of a change in control would constitute a “parachute payment” as defined under Section 280G of the Code, then the benefits payable will be reduced to $1 below the parachute limit.

Further discussion of the agreements with Messrs. White, Huffines and Salmans, including the definitions of “cause” and “disability” under such arrangements, as well as potential payments made pursuant thereto may be found under the headings “Executive Compensation — Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table” and “Executive Compensation — Potential Payments Upon Termination or Change-in-Control” below.

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Incentive Plans

The 2012 Equity Incentive Plan, under which we have granted awards to the NEOs, contains specific termination and change in control provisions. We determined to include a change in control provision in the plan to be competitive with what we believe to be the standards for the treatment of equity upon a change in control for similar companies and so that employees who remain after a change in control would be treated the same with regard to equity as the general stockholders who could sell or otherwise transfer their equity upon a change in control. Under the terms of the 2012 Equity Incentive Plan, if a change in control (as defined below in the discussion of the plan under "Executive Compensation — Potential Payments Upon Termination or Change-in-Control") were to occur, all awards then outstanding would become vested and/or exercisable and any applicable performance goals with respect thereto would be deemed to be fully achieved. Further discussion of the change in control payments made pursuant to the 2012 Equity Incentive Plan may be found in the "Executive Compensation — Potential Payments Upon Termination or Change-in-Control" section below.

The Annual Incentive Plan, pursuant to which annual incentive bonuses are awarded, does not contain specific change in control provisions. Accordingly, the Committee, in its discretion, may determine what constitutes a change in control and what effects such an event may have any awards made pursuant to such plan.

Risk Considerations in Our Compensation Program

We do not believe that our compensation policies and practices for 2015 give rise to risks that are reasonably likely to have a material adverse effect on our Company. In reaching this conclusion for 2015, we considered the following factors:

- Base salary is fixed and the only compensation components that are variable are the annual incentives and performance-based RSUs awarded to NEOs, which were awarded based upon attainment of pre-determined levels of earnings.
- Annual Incentive Plan payments to the NEOs were determined or approved following the substantial completion of the audit of the Company's consolidated financial statements by the Company's independent registered public accounting firm. Thus, the Committee had ample knowledge of the financial condition and results of the Company, as well as reports of other committees of the Board of Directors, upon which to base any decisions.
- We have a balanced program that includes multiple performance goals, rewards short and multi-year performance, pays in cash and equity and provides a meaningful portion of pay in stock, which is tied to our long-term performance.
- The Annual Incentive Plan awards are subject to claw-back and adjustments for improper risk and significant compliance issues.
- Each year the Committee reviews all compensation programs to ensure existing programs are not reasonably likely to have a material adverse effect on the Company.

Other Programs and Policies

Stock Ownership Requirements

In February 2014, the Committee recommended, and the Board of Directors adopted, a stock ownership policy applicable to our executive officers and directors. Within five years of the later of appointment or the date the policy was adopted, executive officers are required to achieve ownership of a defined market value of Company common stock equal to a minimum number of equity or equity-based securities as follows:

- Six times annual base salary for the Chief Executive Officer; and
- Three times annual base salary for the other executive officers.

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Under this policy, directors are expected to own shares with a value greater than five times their annual retainer for serving on the Board of Directors of the Company. Our director compensation program permits directors to elect to receive their director compensation in cash, Company common stock or a combination of cash and Company common stock.

In calculating equity ownership for purposes of this requirement, we will include all shares beneficially owned by an individual, such as shares owned by an individual in the Company's benefit plans (e.g., 401(k)), shares of restricted stock and shares with respect to which an individual has voting or investment power. Shares underlying unexercised stock options and unearned performance shares are excluded when determining ownership for these purposes.

Executive officers are expected to hold 50% of any net shares received through compensatory equity-based grants until the ownership guidelines are achieved. Once such officer achieves the ownership requirement, he or she is no longer restricted by this holding requirement; provided his or her total stock ownership level does not fall below the ownership guidelines.

In addition, all awards of RSUs granted since February 2014 to NEOs are, subject to certain exceptions, required to be held for one year after vesting.

As of April 1, 2016, all NEOs and a substantial number of directors are on track to meet the ownership guidelines. Directors who are restricted from receiving stock pursuant to their current employment arrangement have been exempted from this requirement.

Clawback Policy

Our compensation program also includes a claw-back from any annual cash or long-term incentive award for improper risk and significant compliance issues. Annual Incentive Plan awards are subject to any clawback, recoupment or forfeiture provisions (i) required by law or regulation and applicable to Hilltop or its subsidiaries or (ii) set forth in any policies adopted or maintained by Hilltop or any of its subsidiaries.

Tax Considerations

Section 162(m) of the Code imposes a $1.0 million limit on the tax-deductibility of compensation paid to our five most highly paid executives, which includes the NEOs. Exceptions are provided for compensation that is

"performance-based" and paid pursuant to a plan meeting certain requirements of Section 162(m) of the Code. The Committee has carefully considered the implications of Section 162(m) of the Code and believes that tax deductibility of compensation is an important consideration. Accordingly, where possible and considered appropriate, the Committee strives to preserve corporate tax deductions. The Committee, however, reserves the flexibility, where appropriate, to approve compensation arrangements that may not be tax deductible to the Company, such as base salary and awards of time-based RSUs. The Committee will continue to review the Company's executive compensation practices to determine if other elements of executive compensation constitute "qualified performance-based compensation" under Section 162(m) of the Code.

Trading Controls and Hedging, Short Sale and Pledging Policies

Executive officers, including the NEOs, are required to receive the permission of the General Counsel prior to entering into any transactions in our securities, including gifts, grants and those involving derivatives. Generally, trading is permitted only during announced trading periods. Employees who are subject to trading restrictions, including the NEOs, may enter into a trading plan under Rule 10b5-1 under the Exchange Act. These trading plans may be entered into only during an open trading period and must be approved by the General Counsel. We require trading plans to include a waiting period and the trading plans may not be amended during their term. The NEO bears full responsibility if he or she violates our policy by permitting shares to be bought or sold without pre-approval or when trading is restricted.

Executive officers are prohibited from entering into hedging and short sale transactions and are subject to restrictions on pledging our securities.

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Compensation Committee Report

The Compensation Committee of the Board of Directors of Hilltop Holdings Inc. has reviewed and discussed with management the Compensation Discussion and Analysis contained in this Proxy Statement. Based on its review, the Compensation Committee recommended to the Board of Directors that the Compensation Discussion and Analysis be included in the Proxy Statement.

The foregoing report has been submitted by the following members of the Compensation Committee:

Haag Sherman (Chairman)	Rhodes Bobbitt	W. Joris Brinkerhoff
William T. Hill, Jr.	Andrew Littlefair	

Executive Compensation

The following tables set forth information concerning the compensation earned for services performed during 2015, 2014 and 2013 by the NEOs, who were either serving in such capacities on December 31, 2015, during 2015, or are reportable pursuant to applicable SEC regulations.

Summary Compensation Table

Fiscal Years 2015, 2014 and 2013

sition	Year	Salary ($)	Bonus (a) ($)	Stock Awards (b) ($)	Option Awards ($)	Non-Equity Incentive Plan Compensation (c) ($)	Change in Pension Value and Nonqualified Deferred Compensation (d) Earnings ($)	All Other Compensat ($)
	2015	662,500 (f)	—	679,741	—	740,000	—	70,861
	2014	537,500 (g)	—	600,013	—	600,000	—	23,028

r	2013	466,667 (h)	—	397,500	—	500,000	—	1,800
	2015	333,750 (f)	—	169,935	—	290,000	—	3,106
nt								
	2014	322,500 (g)	25,000 (i)	175,004	—	300,000	—	3,318
ficer	2013	296,667 (h)	—	66,250	—	200,000	—	1,800
	2015	1,350,000	1,350,000	679,741	—	—	29,261	110,142
r of	2014	1,350,000	1,350,000	699,991	—	—	29,129	106,142
ion	2013	1,350,000	1,350,000	662,500	—	—	28,950	132,877
	2015	690,000	—	407,849	—	555,000	—	41,824
	2014	690,000	—	420,000	—	555,000	—	41,433
ion	2013	690,000	—	397,500	—	555,000	—	41,564
	2015	750,000	—	339,871	—	1,000,000	—	53,292
r of	2014	750,000	500,000	350,008	—	500,000	—	34,967
	2013	750,000	—	331,250	—	—	—	31,906

(a) Represents bonuses paid for services during 2015, 2014 and 2013, as applicable.

(b) Reflects the grant date fair value calculated in accordance with the provisions of the Stock Compensation Topic of the ASC. The value of performance-based stock awards is based on the probable outcome of such performance conditions. The following table presents the value of performance-based awards based on the achievement of both probable and maximum outcomes:

		Performance-Based Stock Awards	
Name	Year	(Probable Achievement) ($)	(Maximum Achievement) ($)
Jeremy B. Ford	2015	332,624	498,936
	2014	234,559	351,838
Darren E. Parmenter	2015	83,156	124,734
	2014	68,413	102,619
Alan B. White	2015	332,624	498,936
	2014	273,633	410,450
James R. Huffines	2015	199,567	299,350
	2014	164,187	246,281
Todd L. Salmans	2015	166,312	249,468
	2014	136,826	205,239

(c) For 2015, represents cash awards earned under the Annual Incentive Plan for services during 2015, but paid in March 2016. For 2014, represents cash awards earned under the Annual Incentive Plan for services during 2014, but paid in March 2015. For 2013, represents cash awards earned under the Annual Incentive Plan for services during 2013, but paid in March 2014.

(d)

Represents interest earned on non-qualified deferred compensation contributions to Mr. White during 2015, 2014 and 2013, as applicable. For additional information, see "— Non-Qualified Deferred Compensation."

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(e) Includes amounts paid during 2015, 2014 and 2013, as applicable, for group life insurance premiums, auto allowance, gym and club expenses, use of a company car and aircraft, and cash incentive payments. The table following these footnotes is a breakdown of all other compensation included in the "Summary Compensation Table" for the NEOs.
(f) Reflects increase in annual salary effective on April 1, 2015.
(g) Reflects increase in annual salary effective on April 1, 2014.
(h) Reflects increase in annual salary effective on April 1, 2013.
(i) Reflects the portion of his bonus pursuant to the Annual Incentive Plan in excess of the maximum stretch bonus permitted thereunder.

All Other Compensation

Name	Year	Perquisites and Personal Benefits (a) ($)	Gross-Ups or Other Amounts Reimbursed for the Payment of Taxes ($)	Company Contributions to Defined Contribution Plans ($)	Insurance Policies (b) ($)	Director Fees ($)	Total All Other Compensation ($)
Jeremy B. Ford	2015	70,081	—	—	780	—	70,861
	2014	22,248	—	—	780	—	23,028
	2013	1,800	—	—	—	—	1,800
Darren E. Parmenter	2015	1,800	—	—	1,306	—	3,106
	2014	1,800	—	—	1,518	—	3,318
	2013	1,800	—	—	—	—	1,800
Alan B. White	2015	100,236	—	—	9,906	—	110,142
	2014	96,236	—	—	9,906	—	106,142
	2013	127,729	—	—	5,148	—	132,877
James R. Huffines	2015	36,676	—	—	5,148	—	41,824
	2014	36,285	—	—	5,148	—	41,433
	2013	36,416	—	—	5,148	—	41,564
Todd L. Salmans	2015	43,386	—	—	9,906	—	53,292
	2014	25,061	—	—	9,906	—	34,967
	2013	22,000	—	—	9,906	—	31,906

(a) Year 2015: For Mr. Jeremy B. Ford, reflects $1,800 gym membership allowance and personal use of company airplane of $68,281. For Mr. Parmenter, reflects $1,800 gym membership allowance. For Mr. White, reflects car

allowance of $36,000, club expenses of $33,921, personal use of company airplane of $28,363, and personal use of company automobile of $1,952. For Mr. Huffines, includes a car allowance of $24,000 and club expenses of $12,676. For Mr. Salmans, includes a car allowance of $12,000, club expenses of $10,000, and cash incentives of $21,386. Year 2014: For Mr. Jeremy B. Ford, reflects $1,800 gym membership allowance and personal use of company airplane of $20,448. For Mr. Parmenter, reflects $1,800 gym membership allowance. For Mr. White, reflects car allowance of $36,000, club expenses of $33,768, personal use of company airplane of $24,617, and personal use of company automobile of $1,852. For Mr. Huffines, includes a car allowance of $24,000 and club expenses of $12,285. For Mr. Salmans, includes a car allowance of $12,000, club expenses of $10,000, and cash incentives of $3,061. Personal use of company aircraft is calculated on a per mile basis utitlizing SIFL rates published by the IRS.

(b) Reflects group term life insurance premiums paid during 2015, 2014 and 2013, as applicable.

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Grants of Plan-Based Awards

Grants of Plan-Based Awards Table

Fiscal Year 2015

		Estimated Future Payouts Under Non-Equity Incentive Plan Awards (b)			Estimated Future Payouts Under Equity Incentive Plan Awards (c)			All Other Stock Awards:	Grant D Fair Va
Grant Date (a)		Threshold ($)	Target ($)	Maximum ($)	Threshold (#)	Target (#)	Maximum (#)	Number of Shares of Stock or Units (d) (#)	of Share a Option Awards (e) ($)
2/24/2015								18,004	347,11
2/24/2015					9,002	18,004	27,006		332,624
3/10/2015		108,000	600,000	750,000					
2/24/2015								4,501	86,779
2/24/2015					2,251	4,501	6,752		83,156
3/10/2015		28,200	235,000	293,750					
2/24/2015								18,004	347,11
2/24/2015					18,004	18,004	18,004		332,624
3/10/2015	(f)	1,350,000	1,350,000	1,350,000					
2/24/2015								10,803	208,282
2/24/2015					5,401	10,802	16,203		199,561
3/10/2015		99,900	555,000	693,750					
2/24/2015								9,002	173,559
2/24/2015					4,501	9,002	13,503		166,312
3/10/2015		90,000	750,000	937,500					

(a) Represents the effective date of grant of RSUs under the 2012 Long-Term Incentive Plan and payment of annual cash incentive awards under the Annual Incentive Plan.

(b) Represent the value of potential payments under the Annual Incentive Plan to the NEOs based on 2015 performance. Management incentive award amounts shown above represent potential awards that may have been earned based on performance during 2015. The actual Annual Incentive Plan awards earned for 2015 are reported

in the "Summary Compensation Table" above. For more information regarding the Annual Incentive Plan, see below and also refer to "Compensation Discussion and Analysis" in this Proxy Statement.

(c) Represents performance-based RSUs that vest based upon the achievement of certain performance goals during the three-year period beginning January 1, 2015 and ending December 31, 2017. These RSUs were issued pursuant to the 2012 Equity Incentive Plan and a form of award agreement and are subject to forfeiture, accelerated vesting and other restrictions as more fully set forth in the 2012 Equity Incentive Plan and the form of award agreement. For additional information, see "— Compensation Discussion and Analysis — Elements of our Executive Compensation Program — Long-Term Incentive Awards."

(d) Represents time-based RSUs that cliff vest upon the earlier of the third anniversary of the date of grant and a change of control. These RSUs were issued pursuant to the 2012 Equity Incentive Plan and a form of award agreement and are subject to forfeiture, accelerated vesting and other restrictions as more fully set forth in the 2012 Equity Incentive Plan and the form of award agreement. For additional information, see "—Compensation Discussion and Analysis — Elements of our Executive Compensation Program — Long-Term Incentive Awards."

(e) Reflects the grant date fair value calculated in accordance with the provisions of the Stock Compensation Topic of the ASC. For more information regarding outstanding awards held by the NEO, refer to section "Outstanding Equity Awards at Fiscal Year-End" below.

(f) Represents the amount Mr. White would be entitled to under his retention agreement.

Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table

Employment Contracts and Incentive Plans

Set forth below is a summary of our retention agreement with Mr. White and our employment agreements with Messrs. Huffines and Salmans. We do not have employment agreements with Messrs. Jeremy B. Ford or Parmenter. Also set forth below is a description of our incentive plans, pursuant to which the awards included in the "Outstanding Equity Awards at Fiscal Year-End Table" below were made to our NEOs. The Compensation Committee believes that the arrangements described below serve our interests and the interests of our stockholders because they help secure the continued employment and dedication of our NEOs prior to or following a change in control, without concern for their own continued employment.

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Employment Contracts

Mr. White

On November 30, 2012, in connection with our acquisition of PlainsCapital, we entered into a retention agreement with Mr. White. The term of the retention agreement is three years, with automatic one-year renewals at the end of the second year of the agreement and each anniversary thereof unless notice has been given otherwise. Pursuant to the agreement, Mr. White's annual base salary is $1,350,000. He is also entitled to an annual bonus that varies based upon the performance of PlainsCapital. If PlainsCapital's annual net income is less than or equal to $70,000,000 but greater than $15,000,000, Mr. White is entitled to a bonus equal to the average of his annual bonus in the prior three calendar years. If PlainsCapital's annual net income exceeds $70,000,000, he is entitled to a bonus equal to 100% of his annual base salary. Additionally, in accordance with the agreement, Mr. White is entitled to participate in all of the Company's employee benefit plans and programs. Further, the agreement provides that the Company will provide Mr. White with the use of a corporate aircraft and an automobile allowance, each at the same level that such benefits were available to Mr. White immediately prior to our acquisition of PlainsCapital. He continues to have bank-owned life insurance and access to the country club that was available to him through PlainsCapital's membership prior to our acquisition of PlainsCapital. The agreement also includes, among other things, customary non-competition, non-solicitation and confidentiality provisions. Mr. White's non-competition and non-solicitation obligations terminate thirty-six (36) months after his termination. For a description of compensation and benefits to which Mr. White is entitled in the event of his termination or a change in control, see "Potential Payments Upon Termination or Change-in-Control" below.

Mr. Huffines

On December 4, 2014, we entered into an employment agreement with Mr. Huffines, pursuant to which Mr. Huffines will continue to serve as President and Chief Operating Officer of PlainsCapital. Mr. Huffines's previous employment agreement expired on November 30, 2014 in accordance with its terms. The current employment agreement with Mr. Huffines has a three-year term and provides that Mr. Huffines is entitled to an annual base salary of $690,000 and is eligible to participate in (1) an annual incentive bonus program adopted by the Compensation Committee and (2) any long-term incentive award programs adopted by the Compensation Committee. Mr. Huffines is also entitled to participate in the employee benefit programs generally available to employees of the Company. The agreement also includes, among other things, customary non-competition, non-solicitation and confidentiality provisions. Mr. Huffines's non-competition and non-solicitation obligations continue for twelve (12) months following the earlier of (i) his termination and (ii) the termination of his employment agreement. For a description of compensation and benefits to which Mr. Huffines is entitled in the event of his termination or a change in control, see "Potential Payments Upon Termination or Change-in-Control" below.

Mr. Salmans

On December 4, 2014, we entered into an employment agreement with Mr. Salmans, pursuant to which Mr. Salmans will continue to serve as Chief Executive Officer of PrimeLending. Mr. Salmans's previous employment agreement expired on November 30, 2014 in accordance with its terms. The current employment agreement with Mr. Salmans has a three-year term and provides that Mr. Salmans is entitled to an annual base salary of $750,000 and is eligible to participate in (1) an annual incentive bonus program adopted by the Compensation Committee and (2) any long-term incentive award programs adopted by the Compensation Committee. Mr. Salmans is also entitled to participate in the employee benefit programs generally available to employees of the Company. Additionally, the agreement provides for a one-time cash bonus of $260,000, which was paid to Mr. Salmans upon execution of the agreement. The agreement also includes, among other things, customary non-competition, non-solicitation and confidentiality provisions. Mr. Salmans's non-competition and non-solicitation obligations continue for twelve (12) months following the earlier of (i) his termination and (ii) the termination of his employment agreement. For a description of compensation and benefits to which Mr. Salmans is entitled in the event of his termination or a change in control, see "Potential Payments Upon Termination or Change-in-Control" below.

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Equity Incentive Plans

On December 23, 2003, we adopted the 2003 Equity Incentive Plan, which provides for the grant of equity-based awards, including restricted shares of our common stock, stock options, grants of shares and other equity-based incentives, to our directors, officers and other employees and certain of our subsidiaries selected by our Compensation Committee. At inception, 1,992,387 shares were authorized for issuance pursuant to the 2003 Equity Incentive Plan. All shares granted and outstanding pursuant to the 2003 Equity Incentive Plan, whether vested or unvested, are entitled to receive dividends and to vote, unless forfeited. No participant in our 2003 Equity Incentive Plan may be granted awards in any fiscal year representing more than 500,000 shares of our common stock.

On September 20, 2012, our stockholders approved the 2012 Equity Incentive Plan, and as a result, our ability to grant new awards pursuant to the 2003 Equity Incentive Plan was terminated. However, all awards that were previously granted and outstanding under the 2003 Equity Incentive Plan will remain in full force and effect according to their respective terms and dividend equivalents may continue to be issued in respect of awards that were outstanding thereunder as of September 20, 2012.

The 2012 Equity Incentive Plan provides for the grant of equity-based awards, including restricted shares of our common stock, RSUs, stock options, grants of shares, stock appreciation rights (SARs) and other equity-based incentives, to our directors, officers and other employees and those of our subsidiaries selected by our Compensation Committee. At inception, 4,000,000 shares were authorized for issuance pursuant to the 2012 Equity Incentive Plan. All shares granted and outstanding pursuant to the 2012 Equity Incentive Plan, whether vested or unvested, are entitled to receive dividends and to vote, unless forfeited. No participant in our 2012 Equity Incentive Plan may be granted performance-based equity awards in any fiscal year representing more than 500,000 shares of our common stock or stock options or SARs representing in excess of 750,000 shares of our common stock. The maximum number of shares underlying incentive stock options granted under the 2012 Equity Incentive Plan may not exceed 2,000,000.

The 2003 Equity Incentive Plan and the 2012 Equity Incentive Plan are administered by our Compensation Committee, which has the discretion to, among other things, determine the persons to whom awards will be granted, the number of shares of our common stock to be subject to awards and the other terms and conditions of the awards. The Compensation Committee also has authority to establish performance goals for purposes of determining cash bonuses to be paid under the incentive plans. Such performance goals may be applied to our Company as a whole, any of our subsidiaries or affiliates, and/or any of our divisions or strategic business units, and may be used to evaluate performance relative to a market index or a group of other companies. Further, the Compensation Committee has the authority to adjust the performance goals in recognition of unusual or non-recurring events. The 2003 Equity Incentive Plan and the 2012 Equity Incentive Plan each provide that in no event will the Compensation Committee be authorized to re-price stock options, or to lower the base or exercise price of any other award granted under such plan, without obtaining the approval of our stockholders.

Stock options granted under the 2003 Equity Incentive Plan and the 2012 Equity Incentive Plan may be either "incentive stock options" within the meaning of Section 422 of the Internal Revenue Code, or nonqualified stock options. Generally, holders of restricted stock will be entitled to vote and receive dividends on their restricted shares, but our Compensation Committee may determine, in its discretion, whether dividends paid while the shares are subject to restrictions may be reinvested in additional shares of restricted stock. Except as otherwise permitted by our Compensation Committee, awards granted under the 2003 Equity Incentive Plan and the 2012 Equity Incentive Plan will be transferable only by will or through the laws of descent and distribution, and each stock option will be exercisable during the participant's lifetime only by the participant or, upon the participant's death, by his or her estate. Director compensation paid in the form of our common stock, whether at our or the director's election, is issued through the 2012 Equity Incentive Plan.

Annual Incentive Plan

On September 20, 2012, our stockholders approved the Annual Incentive Plan, which provides for a cash bonus to key employees of Hilltop and our subsidiaries who are selected by the Compensation Committee for participation in the plan. The Annual Incentive Plan is intended to permit the payment of amounts that constitute "performance-based compensation" under Section 162(m) of the Internal Revenue Code and is designed to reward executives whose performance during the fiscal year enabled Hilltop to achieve favorable business results and to assist Hilltop in attracting

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and retaining executives. A participant may receive a cash bonus under the Annual Incentive Plan based on the attainment, during each performance period, of performance objectives in support of our business strategy that are established by our Compensation Committee. These performance objectives may be based on one or more of the following criteria:

- stock price
- earnings (including earnings before interest, taxes, depreciation and amortization)
- earnings per share (whether on pre-tax, after-tax, operations or other basis)
- operating earnings
- total return to shareholders
- ratio of debt to debt plus equity
- net borrowing
- credit quality or debt ratings
- return on assets or operating assets
- asset quality
- net interest margin
- loan portfolio growth
- efficiency ratio
- deposit portfolio growth
- liquidity
- market share
- objective customer service measures or indices
- shareholder value added
- embedded value added
- loss ratio
- expense ratio
- combined ratio
- premiums
- premium growth
- investment income
- pre- or after-tax income
- net income
- cash flow (before or after dividends)
- expense or expense levels
- economic value added
- cash flow per share (before or after dividends)
- free cash flow
- gross margin
- risk-based capital
- revenues
- revenue growth
- sales growth
- return on capital (including return on total capital or return on invested capital)
- capital expenditures
- cash flow return on investment
- cost
- cost control
- gross profit
- operating profit
- economic profit
- profit before tax
- net profit
- cash generation
- unit volume
- sales
- net asset value per share
- asset quality
- cost saving levels
- market-spending efficiency
- core non-interest income
- change in working capital

The performance objectives may be applied with respect to Hilltop or any one or more of our subsidiaries, divisions, business units or business segments and may be applied to performance relative to a market index or a group of other companies. The Compensation Committee may adjust the performance goals applicable to any awards to reflect any unusual or non-recurring events.

Participation in the Annual Incentive Plan does not guarantee the payment of an award. All awards payable pursuant to the Annual Incentive Plan are discretionary and subject to approval by our Compensation Committee. After the performance period ends, the Compensation Committee will determine the payment amount of individual awards based on the achievement of the performance objectives. No participant in the Annual Incentive Plan may receive an award that exceeds $10,000,000 per year. Except as otherwise provided in a participant's employment or other individual agreement, the payment of a cash bonus to a participant for a performance period will be conditioned upon the participant's active employment on the date that the final awards are approved by the Compensation Committee. We may amend or terminate the Annual Incentive Plan at any time.

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Outstanding Equity Awards at Fiscal Year End

The following table presents information pertaining to all outstanding equity awards held by the NEOs as of December 31, 2015.

Name	Number of Securities Underlying Unexercised Options Exercisable (#)		Unexercisable (#)	Option Exercise Price ($)		Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)		Market Value of Shares or Units of Stock That Have Not Vested (a) ($)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)		E P M P U S o T V (a
Jeremy B. Ford	500,000	(b)	—	7.70	(c)	11/2/2016	—		—	—		-
	—		—	—		—	30,000	(d)	576,600	—		-
	—		—	—		—	12,696	(e)	244,017	12,696	(f)	2
	—		—	—		—	18,004	(g)	346,037	18,004	(h)	3
Darren E. Parmenter	—		—	—		—	5,000	(d)	96,100	—		-
	—		—	—		—	3,703	(e)	71,172	3,703	(f)	7
	—		—	—		—	4,501	(g)	86,509	4,501	(h)	8
Alan B. White	—		—	—		—	50,000	(d)	961,000	—		-
	—		—	—		—	14,812	(e)	284,687	14,811	(f)	2
	—		—	—		—	18,004	(g)	346,037	18,004	(h)	3
James R. Huffines	—		—	—		—	30,000	(d)	576,600	—		-
	—		—	—		—	8,887	(e)	170,808	8,887	(f)	1
	—		—	—		—	10,803	(g)	207,634	10,802	(h)	2
Todd L. Salmans	—		—	—		—	25,000	(d)	480,500	—		-
	—		—	—		—	7,406	(e)	142,343	7,406	(f)	1
	—		—	—		—	9,002	(g)	173,018	9,002	(h)	1

(a) Based upon the closing price of $19.22 for our common stock on December 31, 2015. With respect to performance-based RSUs, the number of shares underlying each award was calculated based on

the achievement of target level performance.

(b) This stock option vested in five equal installments on each of November 2, 2011, 2012, 2013, 2014, and 2015.

(c) Represents the exercise price of stock options held by Mr. Jeremy B. Ford, which is the average of the high and low sales prices of Hilltop common stock on the date of grant of the stock option.

(d) Represents shares of restricted common stock that cliff vested on April 1, 2016.

(e) Represents time-based RSUs that cliff vest upon the earlier of February 24, 2017 and a change of control.

(f) Represents performance-based RSUs that vest upon the achievement of certain performance goals during the three-year period beginning January 1, 2014 and ending December 31, 2016.

(g) Represents time-based RSUs that cliff vest upon the earlier of February 24, 2018 and a change of control.

(h) Represents performance-based RSUs that vest upon the achievement of certain performance goals during the three-year period beginning January 1, 2015 and ending December 31, 2017.

Option Exercises and Stock Vested in 2015

During the fiscal year ended December 31, 2015, none of our NEOs exercised any options to purchase shares of common stock or held any outstanding awards of restricted stock, RSUs or similar instruments that vested.

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Non-Qualified Deferred Compensation

The following table shows the non-qualified deferred compensation activity for our NEOs during the fiscal year ended December 31, 2015.

Name	Executive Contributions in Last Fiscal Year ($)	Registrant Contributions in Last Fiscal Year ($)	Aggregate Earnings in Last Fiscal Year (a) ($)	Aggregate Withdrawals/ Distributions ($)	Aggregate Balance at Last Fiscal Year End ($)
Jeremy B. Ford					